

AN ASTHENIC SYMPTOM-COMPLEX.

Its diagnosis and treatment
and relationship to the Supra Renal Gland.

by

Alexander James Muirhead, M.B., Ch.B.

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INDEX.

Terminology	Page	1.
Introduction	Page	2.
History of the Supra Renal Gland.	Page	4.
Anatomy of the Supra Renal Gland.	Page	38.
Physiology of the Supra Renal Gland and the actions of Adrenaline.	Page	42.
Pharmacology of Adrenaline and the Supra Renal Gland.	Page	47.
Pathology of the Supra Renal Gland and a description of the typical symptoms of Addison's Disease.	Page	51.
Symptoms of the Asthenic Symptom-Complex.	Page	62.
Diagnosis of the Asthenic Symptom-Complex.	Page	69.
Prognosis of the Symptom- Complex.	Page	67.
Treatment of the Symptom- Complex.	Page	72.
Case Records of the Symptom- Complex.	Page	73.
Summary.	Page	198.
Conclusion.	Page	216.

Terminology.

Adrenalin or Adrenin after Schafer. or Epinephrin..	The trade name for the pressor principles of the Supra renal gland, isolated by Tekamine.
Adrenals.	Supra Renal Glands.
Asthenia.	Lack of strength and vitality, the "fatigue syndrome"
Cachexia.	The symptoms of severe malnutrition, as seen in the end results of a case of cancer or other serious wasting disease.
Hormone.	A chemical messenger, which formed in one organ, travels in the blood stream to the other organs of the body, and effects a correlation between the activities of the organ of origin and the organs upon which they have their action.

INTRODUCTION.

The scope of this Thesis is limited to a preliminary study of the History, Physiology, and Pathology of the Adrenal Gland, and to the clinical aspect of a "symptom complex" which appears to be due to a hypo-function of the gland; to the treatment of this "complex" by giving of gland extracts per os, and finally to the deductions which have been drawn from the results obtained from the clinical observations both with regard to symptoms and to treatment.

The following procedure has been adopted.

A study of the literature has been made, and a short history of the gland has been condensed therefrom. From these facts, the physiological properties of the gland, so far as they are known, have been extracted. The same method was applied to the Pathology of the Gland.

The clinical investigation was conceived in the following way.

It is known that Addison's disease with its typical symptoms, is almost invariably fatal, and it is due to the most extreme form of dys-function of the Supra Renal Gland.

It is therefore concluded that healthy Supra Renal Glands give off a normal amount of secretion which is necessary to the maintainance

of the normal functions of the body.

If this conclusion is regarded as a mathematical problem, it can be supposed that:-

$\frac{N}{90}$ amount of extract equals Addisons Disease

and $\frac{N}{1}$ amount of secretion equals $\frac{N}{1}$ amount of health,

it would be difficult to deny that between the figures of

$\frac{N}{90}$ amount of secretion equals Addison's Disease, with its typical symptoms, that there must be certain typical symptoms also for:-

$\frac{N10}{20}$ of secretion and $\frac{N}{20}$ and $\frac{N}{30}$ and so on.

For the past five years I have been following certain lines with a view to discovering which are the typical symptoms of the simplest forms of Hypo-functions of the Supra Renal Glands.

HISTORY.

1849. Nothing seems to have been known before this time, about the Adrenal Glands, except their anatomical relations. It was in this year that Addison¹ first published in the London Medical Gazette an account of the clinical condition associated with the destruction of these glands.

This clinical entity, characterised by low Blood Pressure, weakness, and pigmentation, at once became a recognised disease, which unfortunately, had nearly always a fatal ending.

1851. These observations were confirmed by the French Clinician, Trousseau³. It was he who first gave the name Addison's Disease to the condition.

1856. In this year, Brown Sequard² announced the result of experiments, which seemed to him quite conclusive, that the secretion produced in the adrenals was necessary to the life of the animals, which were the subject of his experiments.

1856-1857. In this year, and also the following year, Vulpian⁴ showed that the experiments of Colin⁵ whereby the cut surfaces of Adrenal Glands were stained blue by means of ferric sulphate, were only limited to the medulla.

It was Vulpian, by his oxidising agents turning the cut surfaces of the gland pink who first attempted to show that the secretion of the gland passed into the blood stream,

1857. Physiologists at once began to try and discover what this substance was, and the first record of a detailed analysis was that made by Cloez and Vulpian.⁶

1862. There seems no further clinical or pathological records on the same lines as those of Addison's until the years 1862 and 1865, when Wilks⁷ and Greenhow⁸ confirmed Addison's original observations.

1865. Henle⁹ made the important discovery that the suprenal medulla could be stained brown by means of chromic acid. He suggested the name 'Chromaffin tissue', a term which is still in use at the present day. From this time onwards, the majority of workers directed their attention to the isolation of this chromogen and many detailed analysis of the capsules were made by Cloez and Vulpian¹⁰ and Marino-Zuco¹¹. It is perhaps not going too far to say that the pioneer chemical work was done by Holm¹² in 1867. This observer extracted the minced glands with weak alcohol, and evaporating this off, he dissolved the residue in water. Basic lead acetate solution was then added to precipitate the proteins.

After filtering the excess off, the reagent was precipitated by passing hydrogen sulphide through the solution. The lead sulphide was filtered off, the chromogen was precipitated by the addition of ammonia. Holm therefore laid the foundations of the method for the preparation of

adrenaline since he showed how to remove the proteins and that the chromogen was precipitable by ammonia.

1885.

Eighteen years later,

13.
Krukenberg repeated this work, and suggested that the substance was allied in constitution to catechol. These observations formed the first suggestions as to the constitution of the substance.

1894.

No new observations were

made until 1894, when Oliver and Schäfer
reawakened interest in this subject by their
injection experiments. These observers stated that
the active principle was confined to the medulla,
was insoluble in absolute alcohol and ether, and
was destroyed by alkalis. it was stable to gastric
juice and dealysable.

1892

Abelons and Langlois

describe the results of double extirpation of the Supra Renal gland; Death invariably followed.

This was confirmed by Heiltgreen and Anderseen

1894.

Schafer and Oliver found

that a decoction of the supra renal bodies when injected into the circulation caused a very great rise of Blood Pressure. The active substance responsible for this rise was limited entirely to the medulla, and the infusion of the cortex had no effect on the blood pressure.

Tekamine succeeded in

isolating this substance and called it Adrenalin.

There can be no doubt that this substance was identical with that obtained by Vulpian Holm and Krukenberg.

1897-1898. ²⁰ Vincent wrote in this year

that Adrenaline played a very important part in the maintainance of Blood Pressure. It was also in this year that Ott ²¹ by his experiments

proved that the injection of supra renal extract caused a relaxation of the Alimentary canal;

but the Physiologist Banch ²² demonstrated that although the alimentary canal as a whole was

relaxed by injections of supra renal extract, the ileo colic internal canal was contracted.

1901. ²³ Langley could get no result on the sweat glands, but could get an increase of secretion from the Pancreas if it was already secreting, but not if it was resting.

Similar experiments with similar results were described by Strekl and Weiss. ^{17.}

1905. ²⁴ Magnus showed that Adrenalin in dilutions of 1 in 20.000.000 was capable of producing inhibition of excised plain muscle.

1905. ²⁵ Elliott supported Banch's experiments and agreed that the injection of Adrenaline caused contraction of the ilio colic canal.

1908. ²⁶ Yukow. showed an increase in gastric secretion .

PHYSIOLOGY.

According to Cannon²⁷ because stimulation of the splanchnic fibres give rise to the discharge of Adrenin, the fact is therefore definitely proved that in the body a mechanism exists, by which **Supra Renal** glands can be made to discharge its stimulating substance into the circulation.

Adrenalin is active in a²⁸
dilution of 1 in 2000.000.000 Cannon

1891. ²⁹ Jacobi describes nerve fibres derived from the splanchnic trunks which were distributed to the adrenal glands.

1897. ³⁰ Biedl found that these fibres conveyed Vasodilator impulses to the glands and he suggested that they were secretory impulses.

³¹ Dreyer and ³² Asher presented evidence in support of this suggestion.

1912. ³³ Joseph and Meltzer used the fact that adrenin circulating in the blood causes dilation of the pupil to prove that stimulation of the splanchnics caused an increase in Adrenal secretion.

1921. ³⁴ Elliott confirmed this experiment and additional proof was brought by Cannon & Baymen, ³⁵ .

1913. ³⁴ Elliott found that artificial stimulation of the splanchnics causes a discharge of adrenin. These results have been confirmed by ³⁶ Folin, Cannon and Denis.

The fact is therefore definitely established that in the body a mechanism exists by which these glands can be made to discharge this peculiar substance promptly into the circulation.

Adrenalin is active 1 in 200 million. ³⁸ Cannon .

³⁷ Cannon & D.De la Pay proved that during emotional excitement an increased amount of adrenalin is secreted.

1911. Cannon and Hoskins³⁸ proved that during pain, an increased amount of adrenalin is secreted and this fact has been confirmed by Anrepp³⁹ and Hitchens⁴⁰, Sloan & Austin⁴¹
 1913. Further confirmatory evidence was added by Levy⁴² and Florovsky⁴³.

1918. Opposition to these experiments was presented by the results of the experiments of Stewart and Rogoff⁴³ but the balance of opinion is undoubtedly in favour of Cannon's results.

 Injections of adrenin into the blood alters the distribution of the blood in the body, driving it from the abdominal viscera into the heart, lungs, central nervous system and limbs.⁴⁴ Cannon.

 The increase of adrenalin in pain, and fear and reage cause a liberation of sugar from the liver and a temporary glycosuria.⁴⁵ Cannon .

 Sugar is liberated from the liver when adrenin is injected into the blood stream.⁴⁶ Cannon.

 Adrenal glands are glands of internal secretion.⁴⁶ Cannon.

 Because the adrenal glands are innervated by autonomic fibres of mid-division and since adrenal secretion stimulates the same activities that are stimulated nervously by this division it is possible that disturbance in the realm of the sympathetic, although initiated by nervous

discharge are automatically augmented, and
prolonged through the chemical effects of
the adrenal secretion. Cannon.

1917. Wheeler & Vincent removed one supra renal of the dog and destroyed the medulla of the other. In several such cases the animal survived although only cortical substance was found on post mortem examination.

1918. Boyd describes the case of a soldier who died suddenly whilst he was on leave. He was apparently well just prior to death. The necropsy revealed his supra renal glands to be large structureless masses, larger than the original glands, and only on the left side could a small area of cortex be found. There was no medullary tissue on either side. This helps to establish the results of experiments in animals that only a small portion of the cortex is necessary for life.

1919. Ascoli and Faginole⁴⁹ describe the following test.

An injection of a 1.in a 1000 solution of adrenalin in normal individuals produces a central blue spot surrounded by a white halo, and this again by a blue area.

The extent of the re-action is diminished by Addison's disease.

1920. A Chaffard and G.Larochi and A Grigaut⁵⁰ state that the adrenal cortex is the seat of cholesterol formation.

1920. Lucilielli⁵¹ when one whole capsule and one half of the other is removed in rabbits the animales die of slow asphyxia, which resembles very much the asphyxia of hypo adrenalism. The half capsule that is left does not compensate for the loss.

1918.

S.W.Little.M.D.Rochester,

publishes the following four cases. The only medication used was Adrenal Cortex in doses of grs.2.

CASE NO.1. T.F. MALE. Married. AGE 28 .

November 1917. A spindle celled sarcoma was removed from the rectum.Prompt recurrence, stools ribbon shaped.

March 1918. Second operation, again prompt recurrence and by April 10th ,stools were again ribbon shaped.

Beginning early in April,1918, grs 2 to grs 8 of Supra Renal Cortex were given daily.

April 18th. Stools circular, size of thumb Patient eats and sleeps well. Wt 138 lbs.

June 3rd. Stools normal in size. Patient says he 'feels fine' and is working twelve hours a day (He is a farmer). Wt 143. lbs.

July 13th. Patient continued to improve until two weeks ago,when his tablets gave out and he omitted to get a fresh supply. The surgeon who referred the case to the present writer reports that the growth is beginning to enlarge again, whereas whilst taking the tablets, it had steadily shrunk, rapidly at first, more slowly later. Wt 140 lbs.

Patient now lost sight of.

CASE No. 2. W.H.C. CANCER OF PROSTATE. AGE 57

May 21st 1918. Operation attempted but abandoned because of extent of growth.

June 15th 1918. Supra renal cortex gr 8 daily commenced.

July 1919. Patient reports, that he would have nothing to complain of, if he did not have to wear a urinal.

CASE NO.3. was treated by the writer with little success for nearly a year, when patient forced the diagnosis by calling marked attention to the brown discoloration of her skin.

She had all the Addisonian symptoms for a year, but had not been diagnosed. Various ductless gland preparations had been tried but with no success.

October 1914. Patient diagnosed. Supra renal Cortex grs. 8. daily commenced.

July 1919. From that time, until the present, patient has been considerably well except for two attacks of Influenca, and when she went too long without the cortex medication. At times, she will go months without the cortex, at others a few weeks, without Cortex serve to produce again the anaemia, the lassitude, the skin discoloration etc.

CASE NO. 4. MRS.L.J.W. AGE 35.

Another case of Addisons disease of mild type.

1918. Diagnosed January 1915. Symptoms relieved by Cortex, if Cortex left off symptoms return, to be again promptly relieved by the resumption of medication.

1917. Had been without her tablets for two

months and came for more because she was
getting tired again, and the brown spots
were coming back.

1921. Results of artificially attempting to produce the symptoms of Hypo function of the Supra renal gland. A resume of the above is given by Stewart.
52

He states that up to the present it has not been possible to reproduce experimentally any well characterised symptoms associated with partial insufficiency.

That changes and profound changes take place when the adrenal tissue is removed below a certain limit is not arguable, for life can no longer be maintained and changes which render death inevitable are surely important.

The experimental evidence has tended more and more to show that the cortex is the part of the adrenal indispensable for life. It is the cortical tissue which alone, or rather, most conspicuously undergoes compensatory hyperplasia when a deficiency is created. The accessory adrenal tissue, which also undergoes hypertrophy under these circumstances consists entirely of the cortex.

Stewart sums up the position at present with the following:-

"It is a curious thing that whilst the great bulk of experimental evidence emphasizes the importance of the cortex without demonstrating any very definite physiological value for the medulla, or at least for its epinephrin secretion, the bulk of clinical writers seem almost to ignore the existence of the cortex.

78

There is no evidence that diminution in the ordinary rate of epinephrin output or even its total suppression can give rise to symptoms, even in physiological emergencies which are supposed to increase the demand for epinephrin".

53

1921. F.de Mira et J Jontes .The spontaneous contractions of the excised duodenum of rabbits from which the supra renals have been removed are very small or absent. The effect is present even in an hour. Controls show it is not due to anaesthetic or shock. The inhibitory action to adrenaline is apparently unaffected. Thus adrenaline by itself was unable to supply the deficiency of the supra renal gland as a whole. On the other hand, supra renal extracts injected after removal of the supra renal gland prevent the appearance of inactivity in the duodenum excised fifteen minutes after the injection. It is suggested that the cortex is responsible.

54

1921. W.E.Kay and S.Brock state that the white adrenal line is a local vosomotor reflex and has no direct relationship to adrenal activity.

55

1921. A.Biedl A patient suffering from irritability of the bladder, profuse perspiration and ^{no}aphylactic swellings and sluggishness of the bowels was made well by supra renal gland whole substance.

1922.

56
A.F.Hurst describes a

successful case of 'grafting' in a case of Addison's disease.

1922.

The diagnosis of asthenia of
57

Endocrine origin. A. Sezary .

Clinical observation

distinguishes two types of endocrine asthenia. The first is characterised by quick muscular exhaustion, by rapid fatiguability. This is the adrenal type. On the ⁿ dynamometer the first few efforts register well, the next few rapidly decline to exhaustion. The second type consists of those cases where muscular force diminishes but without rapid exhaustion. A woman seen by the author had a syndrome of painful adiposity and an intense asthenia, which had obliged her to keep her room for a dozen years. She could compress the dynamometer for some time without complete exhaustion. Adrenal extract produced but little improvement, but Thyroid administration affected a remarkable improvement in her.

1922.

In acute infectious diseases, such as Diphtheria, there may be cloudy swelling necrosis and infiltration of the gland, and acute haemorrhage necrosis may take place in the medullary portion of the gland. The same occurs in enteric fever, pneumonia, erysipelas and purpura.

In cholera and diphtheria it has been found that the amount of adrenaline yielded by the medulla is much diminished.

20

Some of the more acute infections and haemorrhagic necrosis are responsible for fatal symptoms of short duration, which may be reasonably attributed to acute interference with the secretory function of the gland. (Taylor.)⁵⁸

1922. Taylor⁵⁹ Simple hypertrophy of the cells of the supra renal cortex gives rise to the following characteristic symptoms.

In women and children, there is adiposity. At the same time, certain male characteristics are seen. Hair grows on the face; there is absence of menstruation and of mammary development. Great muscular strength is developed producing the so-called Infantile Hercules type in male children. There is also great sexual precocity.

1922. Treatment of Addison's Disease, the administration of supra renal preparations or of epinephrin is followed by beneficial and even curative effects, The striking improvement of the asthenia has been demonstrated ergographically. Restoration of the Blood Pressure to normal, disappearance of the hypo-thermia, cessation of the diarrhoea and increase of weight are amongst the other favourable effects noted.

1922. L.V.Kear⁶⁰ Histories are given of three female patients as typifying a large class in whom more or less pronounced thyroid manifestations are accompanied by apparent inadequacy of the

27.

adrenals. Treatment by means of adrenal preparations brought relief, particularly of psychic disturbances.

The author concluded that a marked emotional upset is often associated with underactivity of the adrenals and as overactive thyroid.

61.
Schäffer observes that in Addison's disease it is probably best to give the whole gland rather than adrenaline alone, since it seems undoubted that many of the symptoms are due at least as much, if not more so, to the cortex than to the medullary insufficiency.

62
1922. Black, Hupper & Rogers gives us the following results:- "Feeding with supra renal whole gland causes a considerable increase in the Iodine content of the Thyroid. No effect was got with adrenaline, and the result is presumable due to the cortex".

63
1922. Hurst describes a case of Addisons' Disease, greatly relieved by transplantation of a foetal supra renal gland. The improvement was lasting. The bronzing of the skin was unaffected.

64
Schäffer observes that animals deprived of their supra renal glands do not show unusual pigmentation. If therefore, pigmentation is due to the loss of these organs, it must be the result of a very gradual destruction by disease.

January 28th 1922. Evelyn E. Hewer describes the results of her experiments on 118 white rats which show that:-

- (1) . The Supra renal cortex plays a part in fat metabolism and in calcium metabolism.
- (2). The Supra renal cortex stimulates the thymus to involution.
- (3). The supra renal cortex controls the gonads in both male and female with respect to both reproductive and interstitial cells.
- (4). The Supra renal acts as a whole in controlling general health, in controlling haemoglobin break down, in regulating the production of lymphocytes, in regulating the production of mast cells and in stimulating the thyroid.
- (5). The supra renal medulla is connected with the formation of megaloblast cells.
- (6). Innoculations with various supra renal extracts appear to lower the resistance of experimental animals.

1922. Lucibelli confirmed his experiments on rabbits.

1922.

Cohoe Among the predisposing

causes of Addison's Disease are depressing conditions of life, prolonged worry or emotional shock, intoxications, alcoholism heredity and infections.

A few cases have been reported in which following some shock or depression, the disease has developed and run an acute course.

69

Cohoe .

The commencing symptoms of Addisons disease are marked apathy, and listlessness and mental depression and increased irritability. The mental processes are retarded and the memory shows signs of impairment, and more or less stubborn insomnia.

The asthenia is very generally regarded as the most characteristic and constant symptom of the disease. In almost all cases it occurs as the earliest indication of the onset. It is a psychic as well as a physical asthenia.

70

Cohoe The symptoms referable to the nervous system may be slight at first, but almost invariably a psychic asthenia develops concurrently with the myasthenia.

A striking apathy and a loss of interest in the ordinary pursuits of life and undue mental fatigue are early features of the syndrome. Such patients are often classed as neurasthenics. Mental depression and increased irritability are common manifestations of the altered psychic.

70.
Cohoe

Asthenia is rarely absent,
but quite frequently cases run their course
with a complete absence of melanoderma.

71

1922. Houssay and Lewis confirmed the results of the experiments of Wheeler and Vincent in 1917.

72

Schäfer 'decapsulated animals readily become fatigued and recover very slowly from fatigue'

73.

1922. Iwabuchi In scurvy, produced by feeding guinea pigs on oats, adrenal changes were noted.

74

1923. Verzar and A.V.Beznak carried out experiments to prove that the cortex of the supra renal gland hypertrophies in the absence of Vitamine "B".

75.

1923. F.A. and W.E.Hartman 'Produce evidence to show that adrenaline is present in the cortex. This is not generally confirmed.

76

1923. E.J.Bannerman and O.M.Holly. There is no evidence that the supra renals are the seat of cholesterine formation.

77

1923. G.Maranon . When the finger is drawn along the skin rapidly and somewhat forcibly a line is produced, whatever the pathological condition of the individual and even in those of health.

78

1924. S.P.Scherer Hypoadrenia is one of the common endocrine manifestations and is an important symptom complex.

1924. F.Verzar, E.Kokas, A.Arway . The normal adrenal cortex is eight or nine times the bulk of the medulla. In the absence of Vitamine B . It is fourteen times as great. This experiment confirms Verzars and Beznak's experiment in 1924.

Addison's Disease treated by a supra renal
80.
transplant . M.Currie

When first seen, this married woman aged 50, weighed only 86 lbs. T.98. P.96. Blood pressure diastolic 90. systolic 80. Abdomen deeply pigmented. Severe pains in head and back, and diarrhoea and vomiting.

Dried supra renal tried, and had no effect. Adrenalin given by hypo-dermic root produced fainting By the mouth, produced no effect. Two months' later, she was nearly moribund and the supra renal of a sheep was transplanted into the deep fascia of the abdomen. This caused supuration and the wound was drained. As patient had shown slight signs of improvement another transplantation was done, this time two supra renals from a sheep were used.

Patient at once began to improve. In three months was able to be out of bed all day. Blood pressure higher and pigmentation clearer.

81
1924. Swale Vincent . " It is now generally conceded that the adrenal cortex is essential to life.

1924. Extracts of the cortex give rise to no immediate specific effects when administered to an animal.

Thus it is clear that the evidence for any definite secretion are nil .

82

This same author 'It has been suggested that Choline is the specific secretion of the adrenal gland' also he writes, 'as to which of the cell contents is to be regarded as the true fore-runner of the secretion, there has been much discussion.

Most writers seem to prefer the doubly refracting lipoid granules.

The question also arises as to whether the lipoid globules are formed by the cortical cells or whether they are only deposited there and formed elsewhere.

Da Costa expresses the opinion that the mitochondria are changed into lipoid. Mullions' view is that the mitochondria themselves are the secretory antecedents of a lipoid substance.

1924. Leonard G. Rowntree read a paper before the Association of American Physicians, Atlanta City, N.J. on May 6th (the paper is published by the Division of Medicine of the Mayo Clinic). In this paper he describes the records of 21 cases of Addison's disease since January 1st 1920, and he compares the results of the treatment given to these 21 cases with the records of 26 patients registered at the Mayo Clinic before that date. The first are referred to as Series 1., the second group to Series, 2.

The following figures are of interest. Taking the whole 47 cases, males were more frequently affected than females in a ratio of 2: 1: The average age at onset was 40 years.

In the relation of previous illness to Addison's Disease, he~~l~~ reports that Influen~~a~~a appears to be the commonest etiological factor. Several patients said that they had never fully recovered, but had continued run down until Addison's Disease was finally diagnosed.

Pneumonia is second on the list, and it, in most instances, appeared as a complication of an Influenca. Clinically, tuberculosis appeared to play a minor part, but tuberculous lesions of the supra renals were found in all cases but one coming to necropsy. There were no other definite etiological factors except perhaps syphilis and fright.

In Addison's original series the duration of the disease was on the average, nine months.

In series 1 of the 13 patients who have died, the average duration of the disease was $16\frac{1}{2}$ months, and there are still 8 living. There are no definite results for Series No.2.

The incidence of the various symptoms was as follows:-

Asthenia, and pigmentation was present in every case. Sometimes the weakness was very marked with little pigmentation and vice versa. The pigmentation of some of the patients cleared up strikingly under specific organo-therapy. Loss of

weight occurred in every case.

Gastro intestinal complaints were present in all the cases. Constipation is common but it is often interrupted by marked diarrhoea for two or three days.

Belching and borborygmi are also present at times.

Pain was vague and of a dull deep aching character, in the epigastrium lumbar region or flanks, sometimes bilateral and sometimes unilateral.

Shock or a condition resembling it was present in several cases.

The skin was soft and free from wrinkling, it lacked dryness and the feeling of detachment from the underlying tissue so frequently encountered in marked emaciation.

The results of laboratory findings in these cases may be summarised as follows:-

Urine. normal in amount and consistently sugar free. Occasional albumin. Re-action constantly acid.

Blood 30mg for each 100 cc in ten; 50 mg or
urea more in four and between 90 and 100 mg
 in two cases.

The fasting blood sugar was in the average below normal.

In 50% of the cases whose gastric contents were studied there was achlorhydria. Total and free acids were low in every case.

Basil metabolic tests did not give any definite result.

Blood. There was no specific anaemia in the majority of cases.

Electro cardiograms showed little interest.

Hepatic function was undisturbed in the two cases investigated.

Records of the Gastric contractions were made by Dr Greene by means of a balloon. Following the ingestion of capsules containing 1 grm of dried whole supra renal gland substance, there was a gradual increase in the amplitude and force of the tonus waves. One half hour later there was definite stimulation with contractions of large amplitude usually called "hunger contractions". Epinephrin by mouth and the dried supra renal cortex did not cause an increase in the gastric contractions. Following the preparation of dried supra renal medulla, however, contraction waves and abdominal pain was observed identically with those produced by the whole gland. Clinically we have found that the cortex is less likely to produce those symptoms than the whole gland, although at times the cortex also seemed to be responsible for abdominal cramps and pains.

The principle of the treatment is by frequent administration of adrenaline hypodermically and of whole gland or cortex by the mouth to the point of tolerance.

Tolerance.

Too much epinephrin by

injection is demonstrated by the onset of general weakness, tremor, palpitation or pounding of the heart; too much cortex or whole gland by the mouth gives rise to gastric or abdominal distress, nausea, vomiting, and intestinal cramps.

All other therapeutic factors which may be of use were employed.

The results of treatment depend on the degree of tolerance.

The greatest difficulty is that in long continued treatment patients are unable to tolerate whole gland by the mouth. It is therefore preferable to administer it on a full stomach. The cortex is more satisfactory and apparently equally effective.

In series 2. most of the patients received no organotherapy.

In series 1.

Four patients received no organotherapy. All died within four months. Five patients received modified organotherapy - four died in a few months, the fifth who received 0.66 grm of whole gland by mouth three times a day and l.c.c. of epinephrin in 1:1000 solution daily by rectum lived sixteen months.

Of the 12 patients on the Muirhead regime five are dead, and seven are living. Of those who died, two did so within four weeks of admission.

Seven patients are still living, and appear

to be improving under treatment.

Dr Rowntree's comment is as follows:-

The results of forced organotherapy have certainly exceeded our expectations in several instances. On the other hand, despite our most thoughtful and continuous efforts, five of the twelve patients died under treatment. The prognosis of Addison's Disease is extremely grave. Only in a certain proportion of cases can marked or lasting improvement be expected or obtained.

At best the treatment can only combat functional insufficiency of the supra renal glands. The treatment probably exerts no influence on the fundamental pathological processes of the Addisonian manifestation. Since nothing better is available the Muirhead treatment should be given a fair trial in every case of Addison's disease, care having been exercised however, to see that the patient's individual tolerance is determined, and given due consideration, and that simultaneously every measure is utilised in combating the associated symptoms and the underlying pathological process.

1924. In latent and still more in severe avitaminosis, hypertrophy of the supra renal capsule occurs, it is assumed that Vitamine "B" influences Cholesterol metabolism through the cortical tissue, of the Supra renal gland.

84

1924. J. Watrim shows that the cortex of the Supra renal gland hypertrophied in guinea pigs infected with B. Coli.

85

1924. L. Castaldi found that feeding young guinea pigs on supra renal cortex produced a very considerable increase in their somatic development. In comparison to untreated controls the animals are heavier and fatter and their skeletons bigger, the hair reaches an unusual length, particularly in females. The administration of the extract does not give rise to toxic or anaphylactic phenomena.

86

1924. Cannon and J. R. Pareira showed that adreanal secretion was increased in fever.

87

1925. S. Ogawa describes the effect of fasting on the Supra renal gland. At the beginning of the fasting the secretion of adrenaline increases, but after eight days the store and the secretion are seriously below normal.

88

1925. Meredith Young. M.D. :-

To take one instance only, out of many, the results achieved by the administration of Adrenoscermin Co in cases of post influenza debility, have been most striking. The restoration to health and well being have excelled that obtained by the

use of ordinary tonics, and it has invariably been well maintained". In cases of neurasthenia I have been led to suggest endocrine treatment by the words of Dr Leonard Williams, who said:-

' I boldly call attention to the practical identity in the symptomatology of the real neurasthenia with that of Adrenal insufficiency'.

1925. W.Langdon Brown (opened the Meeting of the Section of Medicine at the Annual Meeting of the British Medical Association 1925, with a Discussion on the Abuses and Uses of Endocrine Therapy) "Before endocrine therapy can claim a rational basis it must be shown that:-

- (1). The gland in question forms an internal secretion.
- (2). The active principle or principles of this secretion can be extracted.
- (3). A method of administration of this extract can be found which will admit of its utilisation by the body.

Referring to Adrenal extract " There is no doubt that the Medulla of the Adrenals yields an intensely active extract. Although this medulla is formed from sympathetic ganglia and adrenaline produced just the same effect on any part as if its post ganglionis sympathetic fibres have been stimulated, it has been urged that these two facts are not connected; and throw no light on the functions of the gland". but this is pushing scientific agnosticism too far when one remembers that the

sympathetic is designed to produce wide spread effects and that these would be assisted by the simultaneous liberation of a chemical stimulant such as adrenaline. I prefer to accept the mass of evidence which points to adrenaline as a general sympathetic stimulant which can be drawn on in an emergency".

"Although we know there is a close association between the cortex and the gonads, I have not seen any definite results from cortical extracts".

89

Swale Vincent 'I have on previous occasions attacked the wholesale uncritical employment of animal products as drugs. But the enemy's line is not yet broken, and the sale of worthless preparations goes on apace.

It is assumed by the physicians who prescribe these products that they all bring about their beneficial results when they are given by the mouth. It is also generally admitted that thryoid and its various preparations are effective when given by the mouth. It is also genarilly admitted that insulin is not of any therapeutic value when given by the mouth. In regard to all the rest (of the organo therapeutic methods), a score of so of much puffed up preparations, there is very considerable doubt. They are only prescribed as organo thereapeutic measures by the most optimistic and uncritical. It is to be noted, however, that this group includes a very large number of

individuals.

With regard to the action of adrenal glands ~~when~~ given by the mouth."Several years ago I fed a hungry dog with the adrenal bodies of a whole flock of sheep, and no effects, could be observed except those of repletion".

90.

1925. Walker. It is possible to transplant the cortex of the supra renal but not the medulla, even if the graft be an auto graft .

1925. Tohuku shows that ether administration exhausts the cats supra renal of its residual adrenaline and this can be prevented by section of the splanchnic nerves.

1925. G M.Stewart and J.M.Rogoff
Dogs survived adrenalectomy for 26 hours to 15 days. There was disorganisation of the digestive metabolism, refusal of food, vomiting, diarrhoea. Blood in vomit or stools, and weakness in hind legs, were among the more marked symptoms. Apparent hallucinations were present with a marked cry.

1926. Starling In his description of the Supra Renal gland writes ' we have very little knowledge of the functions of the cortical portion of these glands.

ANATOMY.

Anatomically, the supra renal glands are two small, flattened bodies of a yellowish colour, situated at the back part of the abdomen posterior to the peritoneum, and immediately superior and in front of the upper end of each kidney; hence one of their names:- supra renal.

They vary in size from $1\frac{1}{4}$ inches to 2 inches in length and are slightly less in width. Their thickness is from two to three lines (4 to 7 mms) whilst their average weight is 60 to 90 grains each. Their size varies greatly, for they are sometimes 'so small as to be scarcely detected' Small accessory glands often surround the adrenals proper and some of the larger of these have both a cortex and a medulla.

The arterial supply to the adrenals is rich and abundant. The blood from the adrenals is carried away by the lumbo-adrenal vein, and is emptied either into the renal vein or directly into the Inferior Vena Cava anterior to the

openings of the Renal Veins.

The nerve supply comes from the
pre-ganglion fibres of the Autonomic group
94.
(Elliott)

HISTOLOGY.

The adrenals consist of two parts- the cortex and the Medulla. The cortex is composed of cells arranged in columns. The outermost layer of cells present an alveolar structure. The lumen, is not very well marked. According to the arrangement of the cells, the cortex is marked off into three distinct zones.

(a). Reticulata, (b) Fasciculata. (c). Glomerulosa.

The cells contain a large amount of granules which give the ordinary re-action for fat but consist probably of lecithin compounds.

The medulla, which is the smaller part of the gland, presents irregular shaped cells, the outlines of which stain darkly with chromates, and give a green colour with salts of iron. It is therefore easy to define the cortex from the medulla.

The supra renals are richly supplied with blood, especially in the medullary part, the cells of which impinge directly on the endothelial lining of the dilated capillaries- but they also receive an abundant nerve supply from the sympathetic system. The glands form a thick meshwork especially in the medulla. (Starling)

DEVELOPEMENT.

The developement of the Human Supra renal gland begins in the embryo at a very early date, and is continued throughout intra uterine life and t the first few years of childhood.

After childhood, the gland acquires features characteristic of the normal Supra renal body. Changes in the Histological structure are observed as age advances, but they are not developemental.
96.
(Eugenia R.A Cooper.)

The gland attains the maximum dimensions
97)
about puberty. (Eugenia R.A.Cooper)

The glands have two distinct tissues,probably differing in the part they play in the animal economy. The cortex is mesoblastic in origon, and the medulla is produced by an outgrowth from the sympathetic system.

PHYSIOLOGY.

The Physiological properties of the Supra renal glands are usually regarded as being identical with those of Adrenin (Adrenalin) This is very far from being a fact, as there is no doubt that the cortex of the gland, which produces no Adrenin has a physiological action, probably more pronouncedⁿ than that of Adrenin.

According to Cooper, the cortex is an important source of lipoid material, but the deepest part of the cortex seems to be further specialised judging from its vascularity.

The meaning of the large numbers of capillaries, and the great amount of connective tissue which forms a matrix for them in the disappearing boundary zone, is not understood, unless the rich area of vascularity is preparing for the developing zona reticularis, which, after the disappearance of the boundary zone has some important function.

Judging from histological appearances, the adrenal seems to be an important source of lipoid material. During later foetal life, the cortex develops rapidly, and produces large quantities of lipoid material, necessitated by the rapid development of the central nervous system.

Some other authorities go so far as to say that the cortex is essential to life. However, as the physiological action of the cortex is a most indefinite one, and of which we have very little knowledge, it is generally said that the physiological actions of the supra renal glands is identical with that of Adrenin. This view, has been so much taken for granted that the cortex is apt to be entirely forgotten; it is therefore essential to remember that when we talk of the physiological properties of the Supra renal glands, we are only talking of the properties of Adrenin.

These properties are identical with the results obtained by stimulation of the sympathetic nervous system, and they may be tabulated as follows:-

- (1) Dilates the Pupil.
- (2) Induces a flow of tears.
- (3) Increases a flow of sweat.
- (4) Profuse salivation.
- (5) Rise of temperature.
- (6) Heart beat violent and interrupted.
- (7) Increase of Respiration rate.
- (8) A rise of Blood Pressure.
- (9) Inhibition of the tone of the small intestines and of the spontaneous rhythm of the muscular walls. (Ott⁹⁸).
- (10) Inhibition of the tone and rhythm of the bladder.

These findings have been upheld to the present day. Dale and Dixon working in conjunction in 1909 conducted experiments which proved that Adrenalin had those properties. Their experiments showed that the rise of Blood Pressure was due to two factors.

(a). by its action on the heart whereby there is an increase in the output and an immediate increase in the frequency and amplitude of the Ventricular beat.

(b). by its action on the arterioles whereby there is a vaso constriction of ~~the~~ pulmonary origon, but there is no constriction of the pulmonary arteries, in fact there is a dilation effect.

Their experiments further proved that adrenalin had the following effect.

On the Spleen.	Contraction.
On the uterus.	Contraction (if pregnant)
On the kidneys.	An increase in the flow of urine.

1919. Cannon's researches showed although an injection of adrenaline causes relaxation of most of the alimentary canal, yet it causes contraction of the ileo colic canal.

1922. Beidl, A German Physiologist showed that an injection of adrenalin caused a rise of temperature.

Langley & Elliott assume that the

action of adrenalin is on some substance between the nerve and the responsive tissue. Langley calls it receptor substance. . Each supra renal receives filaments from the splanchnic nerve on its own side. These end in the medulla without the interposition of any ganglion cells on their Course (Elliott). Stimulation of the peripheral end of the splanchnic nerve causes a discharge of adrenalin into the blood. Through the splanchnic nerve a discharge of adrenalin can be excited by many general conditions, such as pressure on the brain, administration of anaesthetics, mental disturbances. Such a discharge is an important element in the adaption to environmental stress, and enables the animal to react for the preservation of its life either by offence or flight.

When adrenalin is injected into the blood stream, the effect is only temporal since it is easily oxidised and is extremely unstable in solution, we conclude it is destroyed by oxidation in the fluids. Adrenalin is thus a typical hormone, a body of comparatively low molecular weight, - having a drug like excitatory action on the specific tissues of the body - easily diffusible and rapidly destroyed after discharging its office. There seems little doubt that adrenalin is a true internal secretion.

On the heart it has a strong augmentor and accelerator influence, whereas a rise of blood pressure causes an increased systolic volume on the

heart- we may find after an injection of adrenaline, and during the height of the rise of blood pressure, that the heart empties itself more effectively than it did before the injection. In the abdomen, intravenous injection of adrenaline, causes complete relaxation of the stomach- small and large intestines but contraction of the ileo colic splinctor.

On the bladder, its effect is identical with that obtained by stimulating the hypogastric nerves. Adrenalin appears to act in the muscular and glandular tissues themselves, as its action may be obtained not only after the destruction of the cord, and sympathetic plexuses but even after time has been allowed for the peripheral fibres to degenerate.

The effect is not altered under these circumstances and it may still produce either relaxation or contraction of muscles according to the original section of the sympathetic on these fibres.

Supra Renal Extract is obtained from the Supra renal glands of animals. It only exists in the Medulla of the supra renal gland.

99

Hale White .

Here again we must remember we are describing the Pharmacology of Adrenalin.

Adrenalin is an alkaloid having the formula

$$\begin{array}{cccc} \text{C} & \text{H} & \text{O} & \text{N} \\ 9 & 13 & 3 & \end{array}$$

It is a light brown or clear white micro-crystalline powder, having a mildly bitter taste and a slightly alkaline re-action. Very slightly soluble in water, and almost insoluble in alcohol, ether and chloroform. It dissolves readily in hot water, but its aqueous solutions when exposed to the air are gradually oxidised, turning pink, and later, brown in colour.

Adrenalin forms salts with acids, its combination with hydrochloric acid being the most satisfactory; this is now in general use in the form of Adrenalin Chloride solution 1 in 1000.

It is incompatible with alkali or alkaline salts, borax, tannic acid, iron salts or silver nitrate. An absence of iron or soluble alkali is essential in all containers and utensils.

Combinations into which adrenalin enters keep best if rendered slightly acid. If merely neutral, oxidation takes place more readily.

There seems to be some evidence that
dessicated Supra Renal gland has been of
value in Addisons Disease. Stevens ¹⁰⁰

Supra renal extract is used in treatment
of Addison's Disease and other wasting
conditions. In combination with Thyroid and
orchitic extract it has been used in cases
of 'Post Influenal debility' with very marked
results.

Adrenalin is used widely in cases of shock or collapse. A considerable number of cases are now on record, in which after heart massage, and artificial respiration had proved ineffectual Adrenalin Chloride solution has been injected directly into the heart, and has revived its action.

In the case of a woman of 47, who collapsed under an anaesthetic, 2.c.c of Adrenalin solution were injected into the heart and it started to act at once; respiration recommenced after a few minutes and recovery resulted.

In the case of a child six months of age, who collapsed after an operation, under chloroform the intra cardiac injection of 0.75 cc of the 1 in 1000 solution brought about recovery, as also did 1.cc similarly injected in a child $2\frac{1}{2}$ years of age who collapsed after a spasm of whooping cough.

In a case of asphyxia neonatorum in which heart massage and artificial respiration proved unavailing, 6 mins of the 1.in 1000 solution were injected into the heart and caused the latter to beat almost instantly.

Adrenalin seems to have been used to advantage in acute febrile conditions, especially in the later stages of febrile diseases, such as pneumonia, diphtheria, typhoid, or scarletina.

Hypodermic injections of Adrenalin Chloride

solution 1 in 1000 in doses of 5 to 10 mm according to the severity of the case, relieves dyspnoea of cardiac disease, at the same time, it increases the output of urine and so diminishes ascites.

In the paroxysm of asthma, adrenalin is employed because of its effect upon the bronchioles. The fact that adrenin relieves these paroxysms has been demonstrated beyond all doubt, though the mode of action is still problematic.

Adrenalin is the best emergency remedy in the asthmatical paroxysms.

Contrary to what might be expected, oft repeated hypodermic doses of Adrenalin do not lead to sustained high blood pressure; a case is on record in which injections have been given regularly for 14 years and the patient's blood pressure remained sub normal.

Adrenalin also proves useful in Hay Fever.

Adrenalin is of service in rhinitis, larynigitis, and pharyngitis.

There are some records of the oral administration of adrenalin chloride solution controlling paroxysms of coughing and allays the vomiting which often occurs in young people. It has been given in the following doses, two drops every three hours for a child of three years, increasing gradually with the age of the child.

Osler & McGrae^{101.}

Rolleston summarises the condition of the supra renal glands in Addison's Disease thus:-

- (1) The fibre caseous lesion due to tuberculosis far the commonest condition found.
- (2) Simple atrophy.
- (3) Chronic intestinal inflammation leading to atrophy.
- (4) Malignant disease invading capsules including Addison's case of malignant nodule compressing the supra renal vein.
- (5) Blood extravasated into the Supra renal glands.
- (6) No lesion of the Supra renal glands themselves but pressure or inflammation involving the semi-lunar ganglia.

The first is the only common cause of Addison's Disease. The nerve cells of the semi lunar ganglia have been found degenerated and deeply pigmented and the nerves sclerotic. The ganglia are not uncommonly entangled in the cicatricial tissue about the Supra renal glands. The chromaffin cells in the sympathetic ganglia and in the abdominal plexuses generally disappear. The cases of extensive destruction of the glands without Addison's Disease are explained by a persistence of the chromaffin structure elsewhere, while extensive involvement of the extra capsular chromaffin system may itself be sufficient to



cause the symptoms, the adrenals themselves being intact.

Other affections of the Supra Renal Glands.

(1) Lesions of the Adrenal Gland. Remarkable changes in the secondary sexual characters have been associated with tumours and other lesions of this part, so called supra renal genital syndrome.

Pseudo-hermaphroditism has been found in connection with hyperphasia of the cortex, as in a case in which the internal organs were those of a female, but the external had male characters. The reverse may occur. Premature puberty with development of secondary sexual characters may appear as early as the fifth or sixth year. After puberty the presence of a tumour may lead to the remarkable condition known in woman as "virilismus" or hersutismus in which a growth of hair occurs on the face, the voice becomes masculine, and the muscular strength may increase.

Later as signs of tumour develop there are emaciation pigmentation and mental changes.

(II) Hyper and Hypo function of the Adrenals.

The state of our physiological knowledge is at present far too uncertain to make it worth while to discuss the clinical vagaries which have been grouped under the terms hyper and hypo epinephrin-aemia.

(III) Haemorrhage. Acute haemorrhagic adrenalitis presents a picture somewhat resembling acute

pancreatitis, a sudden onset with pain, vomiting, profound prostration, and death within a few days. In other cases convulsions occur, or the patient falls into a typhoid state with profound asthenia. In children the disease may be associated with purpura, both cutaneous and visceral.

(IV) Tumours. Both carcinoma and sarcoma have been described. They are apt to undergo a fatty degeneration and haemorrhage so that they may form very large cysts. In children excessive development of the genitals with hair and fat has been found, as noted by Bullock and Sequeira who collected a number of cases. On this account a suggestion has been made that the adrenal cortex has an hormonal internal secretion which influences sexual development.

(V) Wm. Pepper (tertius) described a form characterised by rapid growth diffuse involvement of the liver and great distention of the abdomen without ascites or jaundice.

The effect of a tumour of the adrenal cortex in childhood is very striking. There is abnormal growth with obesity, precocious sexual maturity,

and excessive growth of hair. It tends to produce virilism in whichever sex it occurs (and it is much commoner in females). The extraordinary condition of chloroma, described by Robert Hutchison, is due to a sarcoma of the adrenal with metastases which particularly affect the skull, and it displays its effect rather as a malignant tumour than by disturbing the endocrine balance.

Defect of the adrenal cortex in childhood produced that rare condition termed progeria by Hastings Gilford. Here the child runs its life-cycle in a few years, and resembles the one described in the "Bab Ballads" who died " an enfeebled old dotard of five". Such facts as these strengthen my suggestion that in childhood the normal function of the adrenal cortex is that of a retarding agent, while playing a more active part at puberty and later. In excess it produces premature maturity; when in defect the life force prematurely fades away and old age supervenes without maturity ever having been reached. For the due succession of the epochs of life, endocrine activities must wax, change and wane in due order.

Fevers, septic conditions, and pneumonia cause a lowering of the content of adrenaline in the Supra renal gland, whilst cases dying from chronic nephritis showed normal figures.

Pathology .

Cloudy swelling haemorrhage and haemorrhagic necrosis is seen in acute infectious diseases, especially diphtheria, and it also occurs in enteric fever, pneumonia, erysipelas, and purpura.

CHARACTERISTIC SYMPTOMS OF ADDISON'S DISEASE.

These are anaemia, general languor, or debility, remarkable feebleness of the heart's action, irritability of the stomach, and a peculiar change of colour in the skin. The onset is, as a rule very insidious.

There are three important symptoms.

(2). Pigmentation of the skin. This as a rule first attracts the attention of the patients' friends. The grade of colouration ranges from a light yellow to a deep brown or even black. In typical cases, it is diffuse, but always deeper on the exposed parts, and in the regions where the normal pigmentation is more intense, such as the areola of the nipples, and about the genitals—also wherever the skin is compressed or irritated as by the waistband. At first it may be confined to the face and hands. Occasionally it is absent. Patches showing atrophy of pigment, leucoderma may occur. The pigmentation occurs on the mucous membranes of the mouth, conjunctivae and vagina, but it is not distinctive as it has been found in chronic gastric disease, and is common in the negro. Over the diffusely pigmented skin, there may be a little mole like spots of deeper pigmentation and upon the trunk, particularly on the lower abdomen, it may be ribbed like the sand on the seashore.

(b). Gastro- Intestinal symptoms. The disease may set in with attacks of nausea and vomiting, spontaneous in character. Toward the close, there may be pain with retraction of the abdomen, and even features suggestive of peritonitis. A marked anorexia may be present. Attacks of diarrhoea are frequent and come on without obvious cause.

(c). Asthenia, the most characteristic feature may be manifested early as a feeling of inability to carry on the ordinary occupation, or the patient may complain of constantly feeling tired. Weakness is specially marked in muscular and cardio-vascular systems. There may be an extreme degree of muscular prostration in an individual apparently well nourished, whose muscles feel firm and hard. The cardio-vascular astenia is manifest in a feeble irregular action of the heart, which may come on in paroxysms in attacks of vertigo- or of syncope in one of which the disease may prove fatal. Blood pressure low- falling to 70 to 80 mm of Hg. Headache frequent symptom; convulsions occasionally occur. Pain in the back may be an early and important symptom. Anaemia a symptom specially referred to by Addison is not common. Blood count usually normal. Sugar contents of the blood found low in some cases. McMunn described an increase in the urinary pigments, and a pigment has been isolated

of very much the same character as the melanin of the skin.

Mode of termination is by syncope which may occur early in the disease- by gradual asthenia- or developement of tuberculous lesions- noisy delirium with urgent dyspnoea may precede fatal event.

Diagnosis. Pigmentation of the skin not confined to Addison's Disease.

The following conditions may give rise to an increase in the pigment, some of which, e.g.

(a) and (b) are due- as in Addison's Disease to disturbance in the chromaffin system.

(a). Abdominal growths- tubercle, cancer or lymphoma. In tuberculosis of the peritoneum pigmentation is not uncommon.

(b). Pregnancy, in which the discolouration is usually limited to the face, the so-called 'masque des femmes enceintes'. Uterine disease is a common cause of a patchy melasma.

(c) Haemochromatosis, associated with cirrhosis of the liver, pigmentation of the skin and diabetes.

(d) In overworked persons of constipated habit there may be a patchy staining of the face and forehead.

(e) The vagabonds discolouration caused by the irritation of lice and dirt may reach high grade, and has been mistaken for Addison's Disease.

(f) In rare instances, there is a deep discolouration of the skin, in melanotic cancer, so general

that it has been confounded with 'melasma suprarenale'.

(g) In certain cases of exophthalmic goitre abnormal pigmentation may occur.

(h). In a few rare instances the pigmentation in scleroderma may be general and deep.

(i). In the face there may be an extraordinary degree of pigmentation, due to innumerable small black comedones. If not seen in a very good light the face may suggest argyria.

Pigmentation of an advanced **grade** may occur in chronic ulcer of the stomach and in dilation of the organ.

(j). Argyria has sometimes been mistaken for Addison's Disease.

(k). Arsenic may cause a most intense pigmentation of the skin.

(l). With arterio-sclerosis and chronic heart disease there may be marked melanaderma.

(m). In pernicious anaemia the pigmentation may be extreme, most commonly due to the prolonged administration of arsenic.

(n). There is a form of deep pigmentation, usually in women which persists for years without any special impairment of health. The pigmentation is a little more leaden than is usual in Addisons' Disease.

(o). In ochondrosis there may be a deep melanotic pigmentation of the face and hands.

(p). In Von Recklinghausen's disease the pigmentation may be uniform and suggestive of adrenal disease.

Where pigmentation is present, these conditions must be sought for, diagnosis for Addison's disease is scarcely justifiable without the asthenia. Difficult to arrive at early conclusion. Important indications - fainting, fits, nausea, gastric irritability.

Prognosis. Disease is usually fatal.

When bronzing is slight or not at all, the case runs a more rapid course. Occasionally acute cases show great weakness, vomiting, diarrhoea and prove fatal in a few weeks. Few cases of disease prolonged to six or ten years. Rare instances of recovery taking place, and periods of improvement lasting many months occur.

Treatment. When asthenia appears, patient should be confined to bed and sudden efforts and muscular exercises should not be allowed. Fatal syncope may occur at any time. For the debility arsenic and strychnine useful. For the diarrhoea, large doses of Bismuth; for irritability of stomach, simple diet and alkalies. Diet light and nutritious, sugar freely given.

As disease is nearly always tuberculous, open air treatment may be carried out. Tuberculin may be tried cautiously, particularly if case is seen early. Operation has been suggested. Lesion is usually localised, and should not be difficult

matter to remove the diseased glands, but so far as we know in animals, this is always a fatal procedure, unless there were supernumary adrenals and a considerable portion of the extra capsular chromaffin intact, operation would be useless.

Adrenal Therapy. Evidently the relation of Addison's Disease to the adrenals is not the same as that of myxoedema to the thyroid gland, in which the insufficiency is promptly relieved by administration of thyroid preparation.

A large number of cases treated with various preparations but very few satisfactory results. Only three of our patients showed marked improvement. One- all severer symptoms disappeared, pigmentation cleared up, but patient died subsequently of an acute infection, which apparently had nothing to do with the disease. Adrenals were sclerosed, but not tuberculous. Dried gland may be given in doses from 5 to 20 grains (0.3 to 1.3 m) three times a day. Epinephrin may be used hypodermically in doses mms 5 to 15 (0.3. to 1.c.c) of the 1 in 1000 solution. Results should be watched carefully.

SYMPTOMS OF THE ASTHENIC SYMPTOMS COMPLEX.

Reliance. These are chiefly subjective. The patients state that they feel unable to make any further effort to carry on their daily work. To them, the slightest effort, even the writing of a letter is the greatest possible burden. On waking in the morning, they are very often as tired as when they went to bed at night, in spite of the fact that they have rested fairly well.

The emotional symptoms are also very marked. Fits of depression lasting from two hours to several days are followed by fits of elation which have no real foundation.

The patients are frightened of trivial things, such as the dark.

They are unable to form their own opinion or hold to it, and are thus liable to doubt their own judgement.

They appear to have no middle course between depression and elation.

They are either deeply depressed about a small worry or highly elated over a small joy.

Sleep is disturbed. The milder forms rest badly, waking several times during the night, and have difficulty in getting to sleep again. In the more severe forms, complete insomnia is present.

The cases I have had under my personal care seem to be able to sleep well for the first

hour to an hour and a half, and it is after this primary rest that the insomnia comes on. Dreams of a terrifying nature occasionally make the already nervous patient almost afraid to go to sleep.

Concentration. The inability to concentrate is another common manifestation. There is a symptom common to several of the more severe cases, I have had under my care, which one is almost unable to define. It appears to be a perversion of the imagination, which causes depression. I will give two concrete instances from my case series, in order to try and bring out what I mean.

One is a married woman, over 40 years of age, who has lived happily with her husband for some 15 years. Every now and again she doubts him.

On close questioning she is unable to say how he has given her any cause, or reason to doubt him; she admits quite frankly that she is absolutely certain, ^{never} he has/been unfaithful to her. This mode of doubt lasts a short while, and after it has passed off she is very remorseful. Before the treatment was commenced, these doubts were becoming frequent; now happily, they are all ended.

The other patient shows the same doubting symptoms with regard to an intimate and close blood relation. Probably the most typical symptom, apart from the nervous symptoms is that

of constipation of a spastic type.

The bowels only act two or three times a week, and then only after the help of purgative pills etc. The shape and colour of the faeces is also characteristic. The faeces are passed in hard small lumps, and frequently cause severe pain at the anus. Most of the patients state that the shape resembles sheep's droppings. The colour is that of a very dark, dull oak stain. Occasionally one has had the direct opposite to constipation, viz many watery stools, but the colour is always very dark and dull.

Case No.3 bears out this, and after treatment the bowels became formed and of a proper colour.

Digestive Tract.

The appetite is usually good, even in severe cases. Flatulence is always present and in the more severe forms borborygmi are very marked.

The Motor System.

Even in the milder forms there is marked muscular weakness. The walking of a mile produces extreme fatigue. There is a disinclination to work or exercise.

Patients generally inform you that they are unable to do as much as they know they could do.

This disinclination is not only confined

to work, it is more often noticeable with regard to sport. For instance, one round of golf is quite sufficient for a keen golfer, although he has plenty of time to play another. A keen cricketer complained that he was only able to bowl two or three overs.

In the more profound cases, the weakness can be so extreme that they are unable to raise themselves from the bed. Pain is not a constant feature, but, when present, it has been situated at the level of the kidney, and is usually referred to by the patient as being over the kidney.

Blood Pressure.

The blood pressure in the cases under review has not been at all typical. The readings have always been done by the Auscultation method. They have not been sufficiently constant in the series of cases to be of use.

According to the physiology of the suprarenal gland, asthenia should be accompanied by a low blood pressure, but this does not always occur, because many cases have been suffering from a prolonged chronic toxæmia, which has given rise to atheroma of the arteries and consequently raised the blood pressure.

Skin Manifestations.

Most cases suffer from urticarical rashes and have very sensitive skins.

They are particularly sensitive to the cold, frequently being unable to get warm, even on the hottest day.

Coldness of the extremities also appears to be rather typical.

Pigmentation.

This is not seen in the milder cases but in one or two of the severer type there was very definite pigmentation chiefly of the mucus membrane of the lips. In two cases there was generalised pigmentation.

The symptom of diminished urinary output has been present in several cases and is always controlled by treatment.

THE PROGNOSIS.

This varies with the underlying causes, but even with such diseases as Cancer, and Tuberculosis, one can, for a period, relieve the patients asthenic symptoms. If the underlying cause can be removed and treatment with the gland extract given, progress is certain.

The results of treatment have been uniformly successful even in cases where there is a definite pathological cause which is not able to be removed.

The effect of treatment in some cases is so sudden that it can be likened to the effect of the relief of pain by large doses of Morphia.

The cases which yield the quickest and best results are the "Post Influenzal Debility Type".

Some cases have to continue taking the treatment continuously, during which time they are perfectly healthy, others have only to take the treatment intermittently to keep well. Experience has taught them when to begin it and when they can safely leave it off. Others, more unfortunate have to keep on continuous treatment and even this only keeps their symptoms in a quiescent state.

In many cases the effect of the treatment may be compared to that of "Thyroid in Myxoedema"

Just as the slow speech and superficial fat of the myxoedematous case disappears in the latter instance, so does the mental lethargy and muscular weakness disappear in this Asthenic group under the influence of supra renal gland extract supplemented by Thyroid.

THE DIAGNOSIS.

The diagnosis of the milder cases depends almost entirely upon the subjective symptoms.

The proceeding of the subjective feeling of muscular fatigue, by the typical mental lethargy already described is very characteristic of this group of symptoms; when there is a combination of these two groups of subjective symptoms, and when on examination no organic cause other than disease of the supra renal gland can be ascertained then it is almost certain that the patient is suffering from this form of asthenia which will at once yield to the treatment by Extract of supra renal gland and small doses of Thyroid.

The patients are very secretive, and it is a great help to the diagnosis when the Physician thoroughly understands what type of emotional symptoms he is likely to encounter, as the patients at once appreciate the fact that the physician understands their case, and is in sympathy with them. They then become very communicative and tell one many facts about themselves, that at first they appear to hide.

The constipation is to be regarded as typical only when the change in the consistency and the colour of the faeces is present.

In severer cases the asthenia will be much more marked, and the mental symptoms will not be so conspicuous . It is at this stage that the primary mental symptoms might be entirely overlooked, because the muscular weakness is inclined to overshadow everything else.

Sergent and others lay stress "On the white adrenal line" as being pathognomonic of this condition, but in the series of cases under review it has not given any specific result.

Ascoli's and Faginole's test also yielded no specific result.

The blood pressure in some cases was very low, but in others it was high. It was consistently low when there was no aparent organic lesion present.

In the most severe group of symptoms there was a close resemblance to Addison's Disease, although only two cases could be definitely put in that category.

It is to be remembered that this asthenic symptom complex may occur in almost any intercurrent disease. The end results of a case of cancer present an almost typical picture of the acute Addisonian syndrome, and the diagnosis can be confirmed in these cases by giving the Gland extracts and testing the results.

If it is true that the Addisonian syndrome is diagnosed by the Profound asthenia and pigmentation, then all cases of astheia with pigmentation

must be classed under this disease.

If, as has been shown by Elliott and others that pain and toxæmia definitely cause a lowering of the secretion of the medulla of the supra renal gland, then there is reason to believe that the typical picture of cachexia may be due to a severe hypo function of the supra renal gland, without there being any definite lesion of the gland.

Experimentally in animals, the Diphtheria toxin causes very marked pathological changes in the supra renal gland. In the human subject, this disease is always accompanied by profound prostration and weakness with a feeble pulse especially as an early symptom. The special points to notice are that in the convalescence of this disease there is a tendency to heart failure and marked depression.

TREATMENT.

The patients which are here reported were all treated with the following prescription:-

Rx

Adrenal Substance Total. gr. $\frac{1}{4}$

Thyroid Gland. gr. 1/12

Spermin Extract. gr. 2

Calcium Glycerophosphate ad gr. 5.

Fiat. "The Tablet".

Sig. One to six daily as required after meals.

In every case a thorough search was made for any underlying pathological cause, and all septic foci, if found, were removed by appropriate means.

Other ordinary methods of treatment were carried out at the same time, but in practically no other case was any other medicant used.

In describing the symptoms of the following cases:-

+ Indicates it is present.

+₁ In a greater degree.

+₂ IN a still greater degree

- Is absent.

± Is sometimes present, and sometimes
absent.

o Not investigated.

Treatment refers to the SPecific Treatment mentioned under that heading.

- With regard to the Blood Pressure indicates a normal systolic pressure for a patient at that age.

+₁ Indicates a high reading and so on.

- Indicates a low reading,

Case No.	1.
Age	
Sex	Male.
Occupation	Small Holder.
Causal Factor	Influenza
Date of onset of symptoms	February 1923
Date of commencing Treatment	June 15th 1923
Date of relinquishing Treatment	June 29th 1923.
Result	Cured.
Duration patient has been under observation :-	Two years.

H I S T O R Y:

June 15th 1923. Since his attack of Influenza, he has felt very fatigued. To put it in his own words: "There is no pleasure in doing anything". He has been unable to play his usual games, simply because he says that he is unable to be bothered to do it.

There is slight shortness of breath on exertion. Sleeping badly. No appetite.

The bowels are opened daily, but are inclined to be very hard, and are passed in small lumps. Again to put it in his own words, "he does not feel fit". He has been under three

Doctors since February, and has had many different forms of treatment trying to get well from this fatigue. He is becoming worried about himself and fears that something else is wrong.

He is highly strung and unable to concentrate.

On Physical examination, nothing was found to be abnormal, except a low blood pressure. His systolic reading was 98 mm HG. The Pulse rate, on examination, after he had done a certain amount of exercise was 76. His temperature 97°. I was unable to obtain the "white line" on stroking.

He was put on to Adreno-Spermin Co. One tablet to be taken four times per day.

June 30th. Very much improved.

He states that at the end of the first day of treatment, he felt an entirely different man, and when he awoke next morning, he was quite his old self again, and at once began to take a pleasurable interest in himself and his surroundings.

He is sleeping well, and his bowels are open daily and are soft and properly shaped. His appetite is good.

On Physical examination his Pulse rate was 90. and blood pressure 110 mm. HG.

April 1925. This patient again returned with minor symptoms and requested to be put on his old treatment. This was done and he immediately improved.

Case No. I

Tabulated Symptoms.

Date	15.6.23	30.6.23	7.7.23			
Muscular Asthenia	+ ₂	+ ₁	±			
Mental Asthenia	+ ₂	—	—			
Amount of Fatigue after slight exercise	+ ₁	±	±			
Constipation	+ ₁	— ₁	— ₁			
Insomnia	±	—	—			
Serjent's "White Adrenal Line"	—	—	—			
Dreams	—	—	—			
Pigmentation	—	—	—			
Paroxysmal Anuria	—	—	—			
Urticaria	+	—	—			
Pulse rate	74.	90	84			
Sensibility to Cold	—	—	—			
Tolerance to Treatment	—	—	—			
Haemoglobin %	88%	90%	0			
Knee Jerks	+	0	0			
Pupil Re-action to light	+	0	0			
Ascoli Test	0	0	0			
Loss of weight	—	—	0			
Gain in weight	—	—	0			
Blood Pressure	S. 98 D. 62	S. 110 D. 70	S. 108 D. 72			

Case No.	2.
Age	56
Sex	Female.
Occupation	Married.no children
Causal Factor	Hereditary.abdominal tumour.
Date of onset of symptoms	November 1921
Date of commencing Treatment	October 30th 1923
Date of relinquishing Treatment	<i>Continuing Dec 1926</i>
Result	A very very great improvement whilst taking the treatment
Duration patient has been under observation	3½ years.

H I S T O R Y:

From Birth, has never been strong. Has never menstruated.

1905. Has a floating kidney.

1919. Pain in right side. Cause not known.

1921. Began to lose strength, and had pain in left side, slightly above the umbilicus. The pain was acute and lasted a month or two. She was confined to bed for eight weeks, at which time, I saw her in conjunction with Dr Titterton, The Hollies, Holbeach, Ipswich. She was in bed, and unable to sit up by herself. She was bronzed; the skin was dry and wrinkled; she was emaciated;

This case is a typical case of Post Influenza Hypo Adrenalism. It yielded at once to treatment with Adreno Spermin Co.

The treatment was only required for two weeks. The insomnia was cured. The slight constipation was cured. The muscular fatigue vanished.

Perhaps the most important element, "that horrid feeling of having no joy in being alive" was at once got rid of by the treatment.

Complained of vomiting, and had fainting attacks. Insomnia was very marked. What sleep she did have was troubled by very bad dreams. The pain in her epigastrium was acute. She was very constipated, and when the bowels did act they were black in colour, very hard, and very lumpy. Her mouth and tongue were dry and parched. She passed practically no urine. Her eyes were dry and hot. She was very depressed, and had given up all hope of recovery. She had been getting gradually worse for the past eight weeks, and had been having various forms of treatment, but with no result.

May 1923. On physical examination, a hard lump, about the size of a pear was discovered over the region of the cardiac end of the stomach. Borborygmi were present, and one could see the ladder pattern of the intestines on the abdominal wall.

The pulse was slow and thready. The blood pressure, systolic reading being 90 mm. HG. The pulse rate was 68. The heart was in a very weak condition. Pigmentation marked.

Both Dr Titterton and myself agreed that she was suffering from carcinoma of the stomach, and was in a very cachectic condition.

As a last hope, I suggested that we try Adreno Spermin Co., and she was given six tablets per day. On seeing her three days

this improvement . She is taking four tablets per day for the last 18 months, and is able to be up and about and do her housework.

She still has periodical attacks of pain and vomiting; she can always tell when these attacks are coming on; Her water ceases, that is she only passes 5 to 6 ounces in twenty four hours; her vision becomes disturbed .

November 1st. She consented to go with me to a clinical Meeting of the B.M.A at King's Lynn in order to assist me as a demonstration case. King's Lynn is 16 miles from her home, but she stood the journey well, although she was very tired the next day.

It occurred to me, that as she had never menstruated, a Thyroid Ovarian Compound might give better results than the Adreno Spermin Co. We therefore started the Thyroid Ovarian Co., but unfortunately this did not do, as she had two attacks of fainting in the afternoon.

November 16th. We re-commenced the Adreno-Spermin Co, and she at once picked up. The bowels became soft; for the past fortnight, they had been lumpy. The urine increased in quantity and she tried to work her sewing machine with her feet.

November 27th. She reports ' I am very pleased to tell you I am feeling very much better this week".

December 1st. She tells me she is much better in every way, and there is no doubt the Adreno Spermin Co is much better than the Thyroid

Ovarian for this case.

She informed me today, that when an attack is coming on, her eyes become very dry and sore, and her mouth becomes very dry and parched.

December 1924. Has had quite a good year. There have been remissions in her symptoms but she has not been confined to bed at all.

December 1925. Has had another good year. The symptoms have been up and down. Just lately the bronzing has been increasing again. Giving single items of the prescription was tried without success (see page)

December 1926. As in 1925. Bronzing still present.

When treatment was commenced this patient was moribund. Within three days this moribund patient was improved.

Three and a half years after, she was able to be up and about her house, and do all her lighter household duties.

There is a tumour in her abdomen, the nature of which, we do not know.

The dry mouth, and sore eyes, and the disturbance of vision are particularly interesting.

The cessation of her urine is always improved by the taking of the tablets, and the amount is at once increased.

Case No. 2

Tabulated Symptoms.

Date	1922	10.5.1922	11.6.22	1923 Dec	1924 Dec	1925 Dec	1926 Dec
Muscular Asthenia		+ ₄	+ ₂	+ ₂	+ ₂	+ ₂	+ ₂
Mental Asthenia		+ ₄	+ ₁	+ ₁	+ ₁	+ ₁	+ ₁
Amount of Fatigue after slight exercise		+ ₄	+ ₃	+ ₂	+ ₂	+ ₂	+ ₂
Constipation		+ ₃	+ ₁	+ ₁	±	- ₁	±
Insomnia		+ ₄	+ ₂	+ ₂	+ ₁	+ ₁	±
Serjent's "White Adrenal Line"		±	±	0	-	-	±
Dreams		-	-	-	+ ₂	-	-
Pigmentation		+ ₃	+ ₂	+ ₂	+ ₁	+ ₂	+ ₁
Paroxysmal Anuria		+ ₃	+ ₁	±	±	-	+ ₁
Urticaria		-	-	-	-	-	-
Pulse rate		60	90	104	108	100	98
Sensibility to Cold		+ ₃	+ ₃	+ ₃	+ ₃	+ ₃	+ ₃
Tolerance to Treatment		+	+	+	+	+	+
Haemoglobin %		44 ⁹ / ₁₀	46	49	54	66	68 ⁹ / ₁₀
Knee Jerks		±	±	0	0	0	0
Pupil Re-action to light		+	+	0	0	0	+
Ascoli Test		0	0	0	-	-	0
Loss of weight		+ ₄	-	-	-	-	-
Gain in weight		-	+ ₁	+ ₁	±	±	±
Blood Pressure		S. 90 D. 64	S. 90 D. 64	S. 112 D. 66	S. 140 D. 88	S. 150 D. 66	S. 144 D. 80

Case No.	3
Age	58
Sex	Male
Occupation	Independent
Causal Factor	Unknown
Date of onset of symptoms	November 1921
Date of commencing Treatment	October 8th 1924.
Date of relinquishing Treatment	
Result	Very much improved. December 1926.
Duration patient has been under observation	25 months.

H I S T O R Y:

In perfect health until November 1921 when he began to feel not quite himself.

November 1922. Diagnosed Auricular Fibrillation.

November 10th 1924. Owing to his own Medical Attendant being away from home, I was asked to see him. On arrival, I found him with an acute pain situated at the right of the umbilicus; he was vomiting. The bowels had been opened with a purge. The urine was a particularly dark colour. This was diagnosed as 'obstructive jaundice' by Dr Robert Hutchison, Devonshire Place, London.

Previous to this sudden attack, the patient had been a complete invalid since 1921 due to auricular fibrillation.

He had been breakfasting in bed, was unable to walk far, and the slightest exertion caused dyspnoea.

He has mental depression. His speech is slow and cerebation sluggish .

The bowels had only been kept open daily by a purge. They had been for many years past, very dark in colour. He had been sleeping badly and feeling that everything he did was scarcely worth while. It was such a tremendous fatigue to think about things. His friends around him were quite concerned.

During his acute attack the urine examination shewed marked excess of urobilin but no bile.

October 9th. His urine still contains an excess of urobilin.

October 10th. Report of the faeces. Except that a few bile pigments were present in small quantities there is nothing abnormal about it.

December 12th. No excess of urobilin present.

February 20th. The bile salts and bile pigments (including bilirubin) are not detected and there is no excess of urobilin.

This patient, for many years previous to this date had suffered from a low Blood Pressure, and a very low temperature. The temperature had been taken daily for a few months in the morning, and

it had never been above 95% and in fact on many occasions, his attendant was unable to read it. There was often attacks of extreme prostration.

I decided to give the patient Adreno-Spermin Co.

I am afraid Dr Hutchison was not very hopeful with regard to this treatment, but he said 'The patient is so seriously ill and so prostrated that if they do good, it would be worth while trying'.

The treatment was commenced on October 8th, 1924, with Adreno-Spermin Co., and all other medicines were stopped. There was an immediate response. The pain cleared up. The yellow colour which we thought was jaundice disappeared. The mental condition became brighter.

Within a month he was up and about. He was able to take a two mile walk with me, and felt none the worse for it, except slightly fatigued.

November 30th, 1924. A symptom which this patient had suffered from for years, was profuse perspiration. This was in no way improved.

December 10th, 1925. He was able to go to London - a journey of 120 miles, and stayed at an Hotel, and went to the Crystal Palace to a Poultry Show.

He went to see the Heart Specialist who had been looking after him and an electro cardiogram still showed auricular fibrillation.

His friends around him, at this time were

absolutely astounded in his change.

His mental outlook being entirely different. The depression and irritability had gone and he has a contented and amiable frame of mind.

2nd December 1925. He has been under treatment until this date, and has kept very well for the past 18 months. He is doing practically everything he wants to do, and he feels more like going back into business than giving it up.

He shoots four to five days a week without any undue fatigue. He sleeps well, and his bowels are opened daily by themselves and are formed and are of a light colour. His face, instead of being bloated and puffy is now firm and the skin smooth instead of wrinkled.

The sub-normal temperature in the morning is improved slightly. The average for the past month is 96. His blood pressure is 90.mm.HG.

He has to continue taking six tablets of Adreno Spermin Compound daily. If he omits to do this he 'at once' has a return of the fatigue; the taking of ^a ~~the~~ tablet removed this sense of tiredness.

December 1926. Has had a very healthy year, not having had one day's sickness. and continues to take his Adreno Spermin Co 6 tablets daily.

Since the commencement of the treatment his bowels act daily without any neccessity for purges. He sleeps much better.

87.
This case showed an instantaneuous
re-action to treatment. The change in his
whole demeanour being very striking.

On the after knowledge of the result
of treatment it seems probable that the acute
attack of pain and etc. which he suffered
in November 1924 might have had a supra renal
basis.

He must continue his treatment.

Case No. 3

Tabulated Symptoms.

Date	1924 Oct 8	Nov. 8 1924	Dec. 8 1924	June 1925	Dec 1925	Dec 1926
Muscular Asthenia	+ ₃	+ ₂	+ ₁	+ ₁	±	±
Mental Asthenia	+ ₃	+ ₂	±	±	±	±
Amount of Fatigue after slight exercise	+ ₄	+ ₃	+ ₂	+ ₁	±	±
Constipation	+ ₂	±	±	±	±	±
Insomnia	+ ₂	+ ₁	±	±	±	±
Serjent's "White Adrenal Line"	+ ₁	+ ₁	+ ₁	+ ₁	+ ₁	+ ₁
Dreams	+ ₁	+ ₁	+ ₁	0	±	±
Pigmentation	—	—	—	—	—	—
Paroxysmal Anuria	—	—	—	—	—	—
Urticaria	—	—	—	—	—	—
Pulse rate	64	66	70	68	66	66
Sensibility to Cold	+ ₂	+ ₂	+ ₂	+ ₁	+ ₁	±
Tolerance to Treatment	+	+	+	+	+	+
Haemoglobin %	69%	78%	82%	78%	76%	81%
Knee Jerks	+	+	+	+	+	+
Pupil Re-action to light	+	+	0	+	0	+
Ascoli Test	0	0	0	0	+	+
Loss of weight	—	—	—	—	—	—
Gain in weight	—	—	—	—	—	+ ₁
Blood Pressure	S 108 D 60	S 104 D 100	S 120 D 68	S 130 D 100	S 162 D 105	S 160 D 100

Case No.	4.
Age	62.
Sex	Female.
Occupation	Retired.
Causal Factor	Overstrain. Mental worries due to business.
Date of onset of symptoms	August 1921.
Date of commencing Treatment	October 1922
Date of relinquishing Treatment	
Result	Very very much improved. December 1926.
Duration patient has been under observation	Four years.

H I S T O R Y:

1900. Appendix removed.

1902. Pyorrhoea. All teeth extracted.

1914. Operation for fixing uterus

October 1922. During the past year, has been subject to very heavy business worries, trying to float a private business into a Limited Company. The venture has not been very successful, this unfortunately followed at the end of 15 years very strenuous life.

Previous to this date, she has always been regarded as a clear headed and very dependable business woman; has been active and successful;

Has had abundant energy - getting up at 7 a.m. and continuing to work physically and mentally until 10 to 11 p.m.

August 1921. She first began to feel the strain of the business worries. This strain was shown by insomnia, and mental irritability, with lack of concentration.

She has been constipated practically the whole of her life, and was in the habit of always taking medicines.

There was a symptom which she had suffered from for years. A periodical stoppage of her urine. For days on end, she would pass little more than 5 to 6 ozs. in 24 hours. She had complained of this symptom to an eminent Physician, but he had offered no suggestion and rather ignored the whole thing. She also complained of it to three other Medical men, who offered no suggestion. She states that when the stoppage occurred, she began to feel run down, depressed, and appeared to be more fatigued than usual, and was certainly more constipated.

Her condition gradually kept getting worse, until she was unable to carry on at all. The constipation became worse, the bowels, when they did act were very hard and lumpy, and of a dark colour. They only acted with purges. The insomnia was worse and she had very bad dreams. Muscular fatigue became prominent. She was unable to walk $\frac{1}{2}$ mile. Her mental condition became worse, she would break

out in tears on the slightest provocation.

She became confused and unable to see things in their proper light. From August 1921 to August 1922, she was under treatment in Edinburgh. Her condition was diagnosed as Neurasthenia, she was advised to rest and take an entire change. She gave up her work. She did this, but did not improve.

October 1922. Physical examination revealed weakened heart sounds, slight dilation of the right border of the Heart. A low blood pressure, viz, 115 mm HG. A slow pulse, 70 after slight exertion. The muscular power, very greatly diminished. The 'red line' obtained by stroking the abdomen was very prominent. Nothing abnormal was found in the abdomen. Nerve reflexes were normal. Her hands and feet were very cold. Sargent's Reflex faintly positive.

Her depression was very great during the consultation. She broke into tears two or three times during the examination.

Treatment with Adreno Spermin Co was commenced six tablets being given daily. On seeing her the following day she said "Thank you so much, I have had the first night's sleep for three years, and something has lifted from my head and I feel quite a different woman!"

This result, after only having two tablets the previous night was astounding. She undoubtedly looked better and there were no

tears at this consultation., and she felt very much clearer in her head, and spoke with more determination and vigour. At the end of a month, she was greatly improved.

The mental depression had practically vanished and the muscular fatigue gradually going, she was able to walk a mile without being tired after it.

She was sleeping 7 to 8 hours a night. The bowels were acting normally every day, without the aid of any purges. They were soft in consistency and light yellow in colour. She has had no return pf the urinary stoppage and has been passing very much larger quantities of water daily.

She began to feel the cold less and her average temperature had risen 1%.

November 1925. This patient has been under observation for three years and taking three to four tablets a day, according to how she feels, and during the whole of this treatment, she has never had any relapse of the stoppage or urine, mental depression or muscular fatigue.

The patient shews some remarkable results.

She stopp d the tablets on October 1st, in order to see how she would get on without them.

At the end of the first week, she felt little different. At the end of the second week, the muscular fatigue came on, her urine ceased, and she began to pass small quantities. At the end of the third week, the muscular fatigue

and the constipation were very marked, depression came on, insomnia was present.

By the end of the third week, she recommenced the tablets and began to feel slight improvement. Her urine at once began to come on in increased quantities. By the end of a week of treatment she was back to her normal condition. Muscular fatigue, depression, and insomnia has entirely disappeared.

This patient entirely demonstrates the rapid action of the tablets viz: While at a Puppy Show she became very tired, and on taking one tablet the tiredness completely vanished and she was able to continue her round, on the exhibition and came home, and was not unduly tired then.

December 1926. Has had a very good year, she still has to continue her treatment, and is unable to continue without it for longer than a fortnight.

Case No. IV.

Tabulated Symptoms.

Date	Oct 4 1922	Dec 1922	Dec 1923	Dec 1924	Dec 1925	Dec 1926
Muscular Asthenia	+3	+3	+2	+2	+1	±
Mental Asthenia	+4	+2	+1	±	±	±
Amount of Fatigue after slight exercise	+4	+2	+1	+1	+1	+1
Constipation	+3	+1	±	±	±	±
Insomnia	+3	+1	±	±	±	±
Serjent's "White Adrenal Line"	+	+	+	+	+	+
Dreams	+3	±	±	±	±	±
Pigmentation	+1	+1	-	-	-	-
Paroxysmal Anuria	+2	+1	-	-	-	-
Urticaria	-	-	-	-	-	-
Pulse rate	70	68	66	72	74	82
Sensibility to Cold	+1	+1	+2	+1	+1	+1
Tolerance to Treatment	+	+	+	+	+	+
Haemoglobin %	80%	84%	82%	74%	90%	92%
Knee Jerks	+	+	+	+	+	+
Pupil Re-action to light	+	+	+	0	0	+
Ascoli Test	0	0	0	0	+	-
Loss of weight	+1	0	-	-	-	-
Gain in weight	-	-	+1	±	±	±
Blood Pressure	5/115 874	5/134 890	5/130 888	5/148 886	5/162 888	5/160 894

Case No.	5
Age	38
Sex	Female.
Occupation	Married. Housekeeper.
Causal Factor	Hereditary Parturition July.1922.
Date of onset of symptoms	July 1922
Date of commencing Treatment	January 1923.
Date of relinquishing Treatment	
Result	Very very much improved. December 1926.
Duration patient has been under observation	Four years.

HISTORY:

1910. Anaemia.

1912. Strained heart. In fact all her life, she has been described as a delicate child.

July 1922. This patient is married, and unfortunately became pregnant. She was delivered of a full time, fine healthy child, but owing to the profound shock, she became very depressed immediately after the birth of the child.

She would not speak to anyone, and would not eat her food. Insomnia was present, and she was continually crying.

This case undoubtedly shews that Hereditary plays a large part in Hypo Adrenalism, as her parents both ~~er~~ suffered from a mild form of Hypo Adrenalism symptoms.

She has had these symptoms all her life.

This case again shows the great benefit derived for sleeplessness and constipation from Adreno-Spermin Co.

On enquiring into her past history, I discovered that she had suffered all her life from constipation. The bowels acting three to four times per week. The constipation was getting worse during the past five years, and she had to take large quantities of medicines. Even with medicine, the faeces were hard and lumpy.

She was described as highly strung, and very nervous - being always terrified of the dark. She was mentally, either very excited or very depressed.

Since her heart trouble in 1912, she had been unable to undertake any heavy physical exertion. The patient began to get worse five days after her baby was born; she was suffering from slight melancholia. By the end of the month, she was feeling very much better.

January 1923. On account of the melancholic condition re-appearing, a course of Adreno Spermin compound treatment was commenced. The result was immediate. She became brighter and says she began to feel well after taking the first few tablets. The insomnia was very much improved within a week of commencing treatment. At the end of a month she was quite a different individual. Her neurasthenic symptoms gradually disappeared, and at the end of the first year of treatment she was quite a different person.

She was sleeping well, had put on weight,

was not so easily fatigued, and did not suffer from fits of depression in the same way.

In order for this patient to keep well, it is necessary for her to continue taking her tablets.

Case No.	Tabulated Symptoms.					
Date	JAN. 1923	MARCH 1923	Dec. 1924	Dec. 1925	Dec. 1926	Feb. 1927
Muscular Asthenia	+ ₂	+ ₁	+ ₁	±	±	±
Mental Asthenia	+ ₄	+ ₂	+ ₁	±	±	±
Amount of Fatigue after slight exercise	+ ₄	+ ₃	+ ₁	±	±	±
Constipation	+ ₄	+ ₁	±	±	±	±
Insomnia	+ ₃	+ ₁	+ ₁	+	+ ₁	+ ₁
Serjent's "White Adrenal Line"	+ ₂	+ ₂	+ ₁	+	+	+
Dreams	+ ₃	+ ₂	±	±	±	±
Pigmentation	+ ₁	+ ₁	+ ₁	±	+ ₁	±
Paroxysmal Anuria	—	—	—	—	—	—
Urticaria	+ ₁	+ ₁	—	—	+ ₁	+ ₁
Pulse rate	68	74	70	68	70	70
Sensibility to Cold	+ ₃	+ ₂	+ ₂	+ ₁	+ ₁	+ ₁
Tolerance to Treatment	+	+	+	+	+	+
Haemoglobin %	74%	82%	88%	80%	86%	86%
Knee Jerks	+	+	+	+	+	+
Pupil Re-action to light	+	0	0	0	0	0
Ascoli Test	0	0	0	0	+	+
Loss of weight	+	—	—	—	—	—
Gain in weight	—	—	+	+	+ ₁	+
Blood Pressure	S, 92 D, 44	S, 100 D, 48	S, 110 D, 48	S, 124 D, 46	S, 130 D, 54	S, 132 D, 56

Case No.

6

Age

44

Sex

Female.

Occupation

Married. one child.

Causal Factor

Hereditary .shock.

Date of onset of symptoms

All her life.
worse since 1919.

Date of commencing Treatment

1922.

Date of relinquishing Treatment

Result

Much improved,
must continue treatment

Duration patient has been under observation

four years.

H I S T O R Y:

1922. This patient first consulted me about a pain which was situated almost directly over the gall bladder. This pain, she said made her feel very weak and very tired. It had been going on for nearly all her life, and she had been under treatment for it some years; a mixture containing Bismuth had given some relief.

She was very constipated, and had those nervous symptoms of alternate depression and excitement. She has told me since, that at times, she was so depressed she thought it would be a

fine thing to commit suicide by hanging herself in the back kitchen.

Her Blood pressure at this time was low. The systolic reading being 108mm HG. The white line obtained on gentle stroking of the skin was very marked.

She was sleeping badly, and was quite unable to walk a mile without very great fatigue.

On physical examination, I found nothing abnormal in the abdomen.

On account of her symptoms, I put her on to Adreno Spermin Co and at once, obtained very gratifying results. The pain disappeared almost immediately, the depression was greatly relieved, and after a week the muscular fatigue had almost vanished.

At the same time, the constipation was cured, and the faeces resumed their normal shape and colour.

This case has been under my observation for nearly three years, and she has been taking the treatment, little or much during the whole of that time.

I am unable to get at the underlying cause, but she seems to have been much worse since the still birth of her baby some three years ago.

The case is interesting, as she is not well off, being only a labourer's wife, and the tablets are expensive. She has, therefore been very

sparing with her treatment, at times, only taking one tablet per day for economy's sake. When she takes the one tablet, she does not feel so well, and her old symptoms return in a minor degree, but when she feels the fit of depression coming on, she at once takes two more tablets, and within ten minutes, the depression vanishes.

This is also true of the pain in her hypo-chondria. As soon as she feels the pain coming on, she takes the tablets, and it is at once relieved. By 'at once' I mean within five minutes. She tells me that if she takes four tablets per day, she feels practically normal.

Her appetite is good, and the bowels opened every day. Sleep is good, and the depression is very slight, and would not be present at all if she took the proper doseage of tablets.

She is now able to bicycle two to three miles without any fatigue at all, and does all her own housework.

Treatment has made no difference to the White Line.

December 1926. In excellent health, has to continue taking the treatment spasmodically.

Case No. V1

Tabulated Symptoms.

Date	1922 Nov	1923 Dec	1924 Dec	1925 Dec	1926 Dec	
Muscular Asthenia	+ ₃	+ ₁	+ ₁	+ ₁	+ ₁	⊕
Mental Asthenia	+ ₄	+ ₁	±	±	±	
Amount of Fatigue after slight exercise	+ ₃	+ ₁	±	±	±	
Constipation	+ ₂	±	±	±	±	
Insomnia	+ ₁	±	±	±	±	
Serjent's "White Adrenal Line"	+ ₂	+ ₂	+ ₁	+ ₁	+ ₁	—
Dreams	+ ₁	+ ₁	+ ₁	+ ₁	±	—
Pigmentation	+ ₁	+ ₁	+ ₁	+ ₁	+ ₁	
Paroxysmal Anuria	±	—	—	—	—	
Urticaria	+	+	—	—	—	
Pulse rate	68	72	74	72	70	
Sensibility to Cold	+ ₂	+ ₁	+ ₁	±	±	
Tolerance to Treatment	+	+	+	+	+	
Haemoglobin %	0	0	0	78	80	
Knee Jerks	+	0	0	0	0	
Pupil Re-action to light	+	0	+	0	+	
Ascoli Test	0	0	0	+	+	
Loss of weight	—	—	—	—	—	
Gain in weight	—	—	—	—	+ ₁	
Blood Pressure	S, 108 D, 66	S, 130 D, 68	S, 138 D, 64	S, 126 D, 68	S, 134 D, 70	

Case No.	7.
Age	74
Sex	Male.
Occupation	Retired. Independent
Causal Factor	Influenca.
Date of onset of symptoms	January 1925
Date of commencing Treatment	June 1925.
Date of relinquishing Treatment	
Result	Cured
Duration patient has been under observation	18. months

HISTORY:

This Patient, previous to January 1925, had enjoyed the very best health. He was a keen sportsman, riding to Hounds, two or three days a week, and shooting.

In January 1925, had a bad attack of Influenca which caused him to be left with profound asthenia. He consulted me in June 1925, From January to June, he had been having treatment with no result. When I saw him, he was complaining of shortness of breath, feeling of chilliness, acute depression, and a lack of inability to concentrate.

He was unable to walk $\frac{1}{2}$ mile without a marked degree of fatigue. He complained of insomnia; after 3.a.m. he would lie awake, thinking and worrying about himself. He was suffering from slight constipation. The faeces were very hard.

On Physical examination, 'heart and Lungs' nothing abnormal diagnosed, except a slight weakness of the heart's action.

Blood pressure 118 mm HG , Urine Nil. White Line was marked.

The pupils reacted to light, and equally.

He has no worries, being in a very comfortable position in life. The reason for the depression, he states is because, he had suddenly become an old man.

Adreno Spermin Co, five tablets daily were ordered. Within a fortnight, he reported a very marked improvement. He wrote me that he felt quite a different man, and almost his old self again.

He was able to take exercise without fatigue and was beginning to ride his horse again, a thing which he had been unable to do since his attack of Influenza in January. He was sleeping much better and his memory had almost returned. Six weeks after having continued the treatment, he wrote me that he was absolutely fit and that he was stopping the tablets.

December 1926. Has remained in excellent health.

Case No. VII

Tabulated Symptoms.

Date	June 1925	July 1925	Dec 1926			
Muscular Asthenia	+ ₃	±	±			
Mental Asthenia	+ ₂	±	±			
Amount of Fatigue after slight exercise	+ ₃	±	±			
Constipation	+ ₁	±	±			
Insomnia	+ ₃	±	±			
Serjent's "White Adrenal Line"	+ ₃	+ ₃	+ ₂			
Dreams	+ ₁	±	±			
Pigmentation	±	±	±			
Paroxysmal Anuria	—	—	—			
Urticaria	—	—	—			
Pulse rate	72	70	74			
Sensibility to Cold	+ ₁	±	±			
Tolerance to Treatment	+	+	0			
Haemoglobin %	0	0	0			
Knee Jerks	+	+	0			
Pupil Re-action to light	+	0	0			
Ascoli Test	0	0	0			
Loss of weight	0	0	0			
Gain in weight	0	0	0			
Blood Pressure	S. 148 D. 100	S. 136 D. 94	S. 148 D. 96			

Case No.	8
Age	53
Sex	Female.
Occupation	Married.multipara
Causal Factor	Tubercular kidney & shock.
Date of onset of symptoms	June 1922
Date of commencing Treatment	March 1923
Date of relinquishing Treatment	
Result	Died 1926.
Duration patient has been under observation	Three years

H I S T O R Y:

1914. Has felt a pain in her left side over her kidney. It used to pass down the ureter into the bladder and pass out through the bladder. The pain continued off and on for seven years, when she began to find herself unable to pass her urine properly.

October 1923. She consulted a Doctor who gave her medicine, but the condition gradually became worse. She started to pass "pieces" in her urine, and this caused great pain. She was sent to Hospital in December 1923 with the diagnosis of a tubercular

kidney. The diagnosis was confirmed in Hospital and an operation was advised. This was absolutely refused, and she went home.

March 1924. She consulted me, and was in a very depressed mental condition,, weeping and crying and insomnia was most marked. What sleep she did get was disturbed by frequent micturition (six to eight times nightly) Blood pressure 110 mm HG White line negative. There was very marked constipation, the bowels being very hard and the colour dark.

She had been in bed for ten weeks.

I informed her that she was suffering from a Tubercular kidney, and that I could not do anything for that, but that I thought I could relieve her pain, and general condition. She was given six tablets daily, and vaginal and bladder douches.

She became very much improved, and in two to three weeks was sitting up in bed. In a month she was up, and in another month, was downstairs, and in August was able to stay up all day.

The micturition at night times had almost ceased, once or twice being the maximum times.

She is able to walk two or three miles. She does most of her own housework, except the scrubbing of the floors, and the washing of the clothes.

She is now able to do with three tablets per day instead of the six.

707.
December 1925. Has had a fairly good year.

April 1926. She died suddrely, becoming unconscious one morning after breakfast, and **dying** within ten minutes.

A Post mortem was refused.

Case No. VIII

Tabulated Symptoms.

Date	1923 MARCH	1923 Dec.	1924 Dec.	1925 Dec.		
Muscular Asthenia	+4	+2	+1	+1		
Mental Asthenia	+4	+1	+1	+1		
Amount of Fatigue after slight exercise	+4	+2	+1	+1		
Constipation	+4	+1	+1	+1		
Insomnia	+4	+1	+1	+1		
Serjent's "White Adrenal Line"	+3	+3	+3	+3		
Dreams	+1	+1	+1	+1		
Pigmentation	+1	+1	+1	+1		
Paroxysmal Anuria	—	—	—	—		
Urticaria	—	—	—	—		
Pulse rate	84	88	86	84		
Sensibility to Cold	+1	+1	+1	+1		
Tolerance to Treatment	+	+	+	+		
Haemoglobin %	72 ⁵ ₆	66	64	68		
Knee Jerks	+	0	0	+		
Pupil Re-action to light	+	0	0	0		
Ascoli Test	0	0	0	0		
Loss of weight	+	+	—	—		
Gain in weight	—	—	+	+		
Blood Pressure	S. 190 D. 120	S. 194 D. 130	S. 198 D. 120	S. 188 D. 124		

Case No.	9
Age	58
Sex	Male.
Occupation	Secretary to Golf Club.
Causal Factor	Acute attack of Influenca. December 1924.
Date of onset of symptoms	Janaury 1925
Date of commencing Treatment	January 1925
Date of relinquishing Treatment	January 1925
Result	Cured. Jan.27th 1925
Duration patient has been under observation	two years.

H I S T O R Y:

January 1925. This patient had an acute attack of Influenca at the latter part of December 1924, which lasted 10 days. Before the attack, he was a strong healthy man doing his Secretarial duties and playing two rounds of Golf daily.

He had had nothing whatsoever the matter with him, and was capable of a good deal of mental exertion. The result of the attack of Influenca was, that he had become depressed, and he was unable to cope with his work, or a book

novel, or paper, because, as he put it, he was too tired to be bothered to look at it.

Muscular weakness was present, insomnia was marked. Bowels acting every day.

On Physical examination, nothing abnormal was found. Pulse rate 76. Morning temperature 98. His urine was clear.

Lungs and Heart, nothing abnormal diagnosed. White Line, Negative.

For a week he was put on Eastern Syrup, and at the end of this time, no result had been achieved, and he was still as fatigued. He was then put on to Adreno Spermin Co four a day.

He informed me, that after taking two tablets, he felt very much better, and began to take an interest in his surroundings again, or as he put it, 'he not only felt better but he also wrote a letter'. He also states he was mentally incapable of doing this on the previous day. The treatment was continued, and within thirteen days, this patient was quite well, and fit to return to his work.

December 1926. Has had no relapse.

Undoubtedly the cause of this Patient's Asthenia was Influenca. He is a most intelligent man , having been a Solicitor in his younger days, and he states definitely that within a very short time of taking the first two tablets, he felt mentally different entirely.

It therefore seems hard to believe that Adreno Spermin Co is not absorbed when taken orally as some observers would have us believe.

Case No. IX

Tabulated Symptoms.

Date	1925 JAN.	1925 Feb.	1925 MAR.			
Muscular Asthenia	+ ₁	±	±			
Mental Asthenia	+ ₂	+ ₁	±			
Amount of Fatigue after slight exercise	+ ₃	+ ₁	±			
Constipation	—	—	—	—	—	—
Insomnia	+ ₂	±	±			
Serjent's "White Adrenal Line"	—	—	—			
Dreams	—	—	—			
Pigmentation	—	—	—			
Paroxysmal Anuria	—	—	—			
Urticaria	—	—	—			
Pulse rate	76	74	74			
Sensibility to Cold	—	—	—			
Tolerance to Treatment	+	+	0			
Haemoglobin %	0	0	0			
Knee Jerks	0	0	0			
Pupil Re-action to light	0	0	0			
Ascoli Test	0	0	0			
Loss of weight	0	0	0			
Gain in weight	0	0	0			
Blood Pressure	S. 154 D. 110	S. 148 D. 104	S. 160 D. 104			

Case No.	10
Age	58
Sex	Male.
Occupation	Retired Colonel.
Causal Factor	Septic infection of the intestines.
Date of onset of symptoms	Many years.
Date of commencing Treatment	December 1924
Date of relinquishing Treatment	December 1925
Result	Very much improved whilst taking treatment.
Duration patient has been under observation	one year.

H I S T O R Y:

1910. Diaphorrea. Cause unknown.

Periodic attacks of sickness ten to
twelve times per month, with intense headache,

This man who has served all his life in the
Army, has been a physically fit man . He is a
keen horseman, a good shot, and a keen Golfer.

He has been suffering many years from
diaphorrea, the cause of which we are unable to
discover. He suffers from intense headaches,
coming on as often as 10 to 12 times a month. These

116.

headaches are so intense, that he requires to lie down on his bed in a darkened room. They are usually followed by vomiting in the morning. During the last few years, he has been gradually failing. He is unable to perform his usual round of pleasures, viz, shooting, golfing, hunting, etc,

He has lost all pleasure in life, and is now unable to play even one round of golf a day, without feeling profoundly fatigued.

He has become very depressed and insomnia is marked. This is quite foreign to his nature.

On physical examination hearts and lungs, nothing abnormal diagnosed. Bowels acting three or four times a day. On bacteriological examination a large number of staphylococci were found to be present.

Abdomen, nothing abnormal diagnosed. The reaction obtained by gently stroking the skin was marked. I advised him to have an autogenous vaccine, colonic lavage, rest and Adreno Spermin Co. He said that in the meantime, he would rather not be bothered with the vaccine, and he certainly would not be bothered with the colon lavage, but he would try the last treatment by itself.

He was therefore ordered six tablets Adreno Spermin Co daily. By the end of the month he was very much improved, and was now able to play his round of golf without fatigue.

His friends remarked how much better and younger he looked. He himself stated that he was beginning to feel fit again. The condition of the bowels had not changed, but had not had any return of sickness or headaches, which was most exceptional for him.

At the end of the second month, he was still improving, and the sickness and headaches had not returned except on one occasion, but this he attributed to a train journey,

December 1925. He has been on treatment, up to the present date, taking four tablets per day. During the whole of this treatment, his bowels had never changed.. He sleeps better and is now able to play two rounds of golf without fatigue, and is now able to carry on his social duties and pleasures as he did ten years ago.

He says that his head aches and sickness have not bothered him at all during the last eight months.

His blood pressure has never altered. The treatment had no effect on the White Line.

Is continuing treatment, but I have no record since last December except that I know he is in his usual health.

Case No. **X**

Tabulated Symptoms.

Date	1924 Dec	Dec 1925	Dec 1926			
Muscular Asthenia	+ ₂	+	+			
Mental Asthenia	+ ₁	+	+			
Amount of Fatigue after slight exercise	+ ₃	+	+			
Constipation	- ₄	- ₃	+			
Insomnia	+ ₁	+	+			
Serjent's "White Adrenal Line"	+ ₂	+ ₂	+ ₂			
Dreams	-	-	-			
Pigmentation	-	-	-			
Paroxysmal Anuria	-	-	-			
Urticaria	-	-	-			
Pulse rate	66	0	0			
Sensibility to Cold	+ ₁	+ ₁	+ ₁			
Tolerance to Treatment	+	+	+			
Haemoglobin %	0	0	0			
Knee Jerks	+	+	+			
Pupil Re-action to light	+	+	+			
Ascoli Test	0	+	+			
Loss of weight	+ ₂	-	-			
Gain in weight	-	+	+			
Blood Pressure	S, 160. D, 90.	S, 162. D, 98.	S, 162. D, 92.			

179

Case No.	11
Age	84
Sex	Female.
Occupation	Nil
Causal Factor	Colitis.
Date of onset of symptoms	Febry 1925.
Date of commencing Treatment	March 1925
Date of relinquishing Treatment	
Result	Very much improved. December 1926
Duration patient has been under observation	20 months.

H I S T O R Y:

April 1924. Mucous Colitis.

March 1925. Two or three times during the Autumn of 1924, this patient became very run down. Up to the present time, in spite of her age, she had been most active, taking a keen interest in all that goes on around her.

She has been constipated all her life, and during the last few years has periodic stoppages of the urine, passing only 5 to 6 ozs daily. This happens about every two months. It is during these attacks, that she feels depressed and fatigued,

and sleeps andly.

The severe illness which she had in 1924, had been completely recovered from, and during the summer, except for constipation, she had no abnormal symptoms.

On account of the success obtained in Case No.4. I tried Adreno Spermin Co for ^{anuria} ~~anuria~~ and on seeing her within two or three days of the commencement, of the treatment, she informed me, that she felt quite a different person, and was much more energetic. She specially noticed that her mind had become clearer, and that she was able to write ~~write~~ letters with some degree of pleasure; previously it had been torture to do these things.

The urinary flow, cleared up.

Unfortunately in April 1926, she developed an acute attack of anuria, together with the most obstinate constipation. She was confined to bed for one month, during which time she had a slight temperature, and also slight vomiting. She became very weak indeed, almost moribund, and for several days, it seemed only a question of hours before she would be dead. There was pigmentation at this time. At this period Adreno Spermin Co was restarted.

For many days previous she had been unable to pass more than 3 to 4 ozs of urine, in spite of the use of energetic diuretics. Within 24 hours of taking Adreno Spermin Co, the urine began to

flow, and on the second day of the treatment she passed 18 ozs of urine, and was gradually beginning to gather her strength. Within a fortnight, she was able to sit up in bed and eat her food.

The treatment was continued and by July 1926, she was able to be downstairs and going about her garden. She still takes the three tablets daily, and is, all things considered in very good health now.

The constipation, although not cured, is very much improved, and during the whole year since her illness she has had no more attacks of anuria.

December 1926. Has had a very good year.

No attack of anuria.

The pigmentation which developed in April 1925 has never properly cleared up.

She continues to take the treatment.

Case No. XI

Tabulated Symptoms.

Date	march 1925	April 1925	April 1926	Dec 1926
Muscular Asthenia	+ ₁	+ ₁	+ ₄	+ ₁
Mental Asthenia	+ ₂	±	+ ₂	+ ₁
Amount of Fatigue after slight exercise	+ ₁	+ ₁	+ ₄	+ ₁
Constipation	+ ₃	±	+ ₃	+ ₁
Insomnia	+ ₁	±	+ ₂	±
Serjent's "White Adrenal Line"	—	—	—	—
Dreams	—	—	—	—
Pigmentation	+ ₁	+ ₁	+ ₂	+ ₁
Paroxysmal Anuria	+ ₃	±	+ ₄	±
Urticaria	—	—	—	—
Pulse rate	76	78	74	72
Sensibility to Cold	+ ₁	+ ₁	+ ₁	+ ₁
Tolerance to Treatment	+	+	+	+
Haemoglobin %	44%	0	0	0
Knee Jerks	+ ₁	+ ₁	+	0
Pupil Re-action to light	+	+	0	0
Ascoli Test	—	—	—	+
Loss of weight	±	±	+	±
Gain in weight	±	±	—	±
Blood Pressure	178.	172. 104	194 90	190 102

Case No.	12.
Age	45
Sex	Female.
Occupation	Housekeeper.
Causal Factor	Unknown.
Date of onset of symptoms	Years ago.
Date of commencing Treatment	23rd May 1924.
Date of relinquishing Treatment	June 1924.
Result	Nil.
Duration patient has been under observation	Two weeks.

H I S T O R Y:

1921. Broken wrist.

Various nervous break downs throughout her life.

This patient did not show the typical symptoms of Hypo Adrenalism, but she did show an acute depression, together with constipation, As a Last resort, I tried Adreno Spermin Co, but she would only have the treatment for a fortnight during which time, we got no results at all.

Case No. XII

Tabulated Symptoms.

Date	May 23 1924	June 14 1924				
Muscular Asthenia	+ ₂	+ ₂				
Mental Asthenia	+ ₃	+ ₃				
Amount of Fatigue after slight exercise	+ ₂	+ ₂				
Constipation	+ ₃	+ ₃				
Insomnia	+ ₁	+ ₁				
Serjent's "White Adrenal Line"	—	—				
Dreams	—	—				
Pigmentation	—	—				
Paroxysmal Anuria	—	—				
Urticaria	—	—				
Pulse rate	70	66				
Sensibility to Cold	+ ₂	+ ₂				
Tolerance to Treatment	+	+				
Haemoglobin %	62%	57%				
Knee Jerks	+	+				
Pupil Re-action to light	+	+				
Ascoli Test	—	—				
Loss of weight	±	±				
Gain in weight	±	±				
Blood Pressure	120 68	118 74				

Case No.	13.
Age	28
Sex	Female.
Occupation	Married. Multipara
Causal Factor	Colitis and fear (a mother's death)
Date of onset of symptoms	1912.
Date of commencing Treatment	April 1923.
Date of relinquishing Treatment	
Result	Very much improved. December 1926.
Duration patient has been under observation	1½ years.

H I S T O R Y:

1912. Colitis for many years. Had first attack in 1912.

Her symptoms as communicated to me by her sister a trained nurse:-

"There is an old standing pelvic pain which keeps her awake five nights out of six, and that, I suppose, accounts in a way for her bad nervous condition. Lately she has had another pain on the other side of her pelvis. For many years she has had colitis which seems to get worse.

There is neuralgic pains in her arms and legs. She has been treated for some considerable period

but there has been no improvement, and the Doctor and the Consultant appear to have lost interest in her, and regard her as a 'chronic', with a certain amount of nervousness. She is a discouraging case I know, but I cannot help thinking of the other poor woman who was labelled 'Chronic' and you may be able to see daylight though my sister's case too.

She is very nervous and my brother-in-law wants me to come with her, when she comes to see you, as ~~she~~ he says he is sure she would not come to your house, unless someone is there to prevent her taking the first train back, without seeing you at all "

March 12th 1923. The above is an extract from a letter written by her sister, and gives a graphic account of the patient's nervous fears, and also clearly indicates the chronic nature of the case.

She complains of a pain in the back, which has been persistent for the past twelve years. She states this is causing insomnia. This pain is worst just previous, and during her menses. She has a great dread of her Mother dying suddenly, and also has been worried. She lost her first baby within one day of its being born. This fear of her mother has led to deep depression. She has periods of depression which cause her to sit down and weep by the hour.

She is very short of breath on exertion, and suffers from severe fatigue after the slightest physical exercise. Her appetite is bad. She says she feels quite out of sorts, and realises her nervous condition acutely.

Physical examination revealed nothing of importance, except that there was marked tenderness over the pelvic colon, which was very distended. Pain was also referred to the upper pole of the right kidney. Blood pressure was low, the systolic pressure being 100 mm Hg. Pulse rate 68. Very sensitive to cold. Urine, nothing abnormal found.

Bacteriological examination of faeces 'Contain some excess of mucus, but we failed to isolate any pathological organism from a series of cultures.'

White line, negative.

P.V. examination, negative.

23rd April 1923. Bowels open once daily for several days, but had two or three days when the bowels were opened two or three times. The pain in her back is very much improved as is the insomnia.

She has lost a great deal of her depression and has ceased to dread her Mothers' condition; she is not now so fearful of some impending calamity.

8th June 1923. Back very much improved, and she is sleeping well. To use her own words:-

"When I think of the sleepless nights and the almost continual backache before I started your treatment, I am most thankful for that much

improvement."

Bowels are troublesome.

7th July 1923. Unfortunately became pregnant in June and is giving up the treatment.

Was delivered of a full time child, which was healthy and she feels well up to date.

December 1926. Has had one or two remissions, but they are always controlled by treatment.

The depression was at once removed,

In spite of the fact that she had been chronically ill for years and that her nerves had given way entirely, she was at once relieved.

The insomnia with troubled and gruesome dreams was replaced by a sound sleep

Pain in the back was entirely cured.

Unfortunately she became pregnant and we were unable to use a vaccine for the treatment of the bowel condition.

Her family were highly delighted with the result.

Case No.

XIII

Tabulated Symptoms.

Date	March 1923.	May 1923.	June 1923.	July 1923.		
Muscular Asthenia	+ ₃	+ ₁	+ ₁	+ ₁		
Mental Asthenia	+ ₃	+ ₂	+ ₂	+ ₁		
Amount of Fatigue after slight exercise	+ ₃	+ ₁	+ ₁	+ ₁		
Constipation	- ₃	- ₁	- ₁	- ₁		
Insomnia	+ ₃	±	±	±		
Serjent's "White Adrenal Line"	-	-	-	-		
Dreams	+ ₃	+ ₁	±	±		
Pigmentation	-	-	-	-		
Paroxysmal Anuria	-	-	-	-		
Urticaria	+ ₁	-	-	-		
Pulse rate	68	74	76	70		
Sensibility to Cold	+ ₃	+ ₃	+ ₁	+ ₁		
Tolerance to Treatment	+	+	+	+		
Haemoglobin %	68%	66%	0	0		
Knee Jerks	0	0	0	0		
Pupil Re-action to light	+	0	0	0		
Ascoli Test	0	0	0	0		
Loss of weight	+ ₂	-	-	-		
Gain in weight	-	+ ₁	+ ₁	+ ₁		
Blood Pressure	S.100	S.98	S.102	S.108		

Case No.	14.
Age	41
Sex	Male.
Occupation	Manager of Wood Factory
Causal Factor	Influenza & shock probably.
Date of onset of symptoms	1918.
Date of commencing Treatment	June 20th 1923.
Date of relinquishing Treatment	September 1923.
Result	Cured.
Duration patient has been under observation	2½ years.

H I S T O R Y:

1918. Valvular Disease of the Heart. D A.H.
Neurasthenia.

1918. Since being in the Army, this patient
had complained of great weakness, Muscular
fatigue coming on after the slightest exertion.

He has been engaged in his work during the
past five years, but it has been a great burden to
do it. Latterly, he has become very depressed.
His depression takes the form of his not wishing
to meet his acquaintances; he could not give any
real reason, why he does not wish to meet them,

except that he just does not want to

He is becoming slightly constipated; the bowels acting four or five times a week. The faeces are hard and lumpy and dark. He is sleeping badly, and has bad night mares. He notices that he is passing a smaller quantity of urine than usual.

Has great difficulty in concentrating in his work.

On Physical examination, nothing abnormal was found; his reflexes were normal.

A red line produced by stroking his abdomen was very very marked. The pulse was slow 68. The blood pressure 120 mm Hg.

His urine contained albumen. The white line reaction, negative.

He was put on Adreno Spermin Co, three tablets daily, and he reports:- "Feeling very much better, a little stronger, and no palpitation. Is now able to walk a mile or two without becoming too fatigued. The bowels have been rather too loose, acting two or three times per day. They are a light yellow colour. The amount of urine has increased very much.

The depression is leaving him, and he is able to meet his friends with proper grace."

At this consultation, the red line produced by stroking his abdomen was very faint. He was advised to continue the treatment.

18th October 1923, He reports:- " Very

much improved. No depression, but had
diahorrea for several days".

Advised to reduce the tablets to two
per day for one month.

16th November 1923. Reports that he
is now his normal self again.

December 1926. Has enjoyed good
health since 1923.

Case No.

XIV

Tabulated Symptoms.

Date	July 1923	Oct 1923	Nov 1923			Dec 1926
Muscular Asthenia	\pm_2	\pm	\pm			\pm
Mental Asthenia	\pm_2	\pm_1	\pm			\pm
Amount of Fatigue after slight exercise	\pm_3	\pm	\pm			\pm
Constipation	\pm_1	\pm	\pm			\pm
Insomnia	\pm_2	\pm_1	\pm_1			\pm
Serjent's "White Adrenal Line"	-	-	-			0
Dreams	\pm_3	\pm	\pm			\pm
Pigmentation	-	-	-			0
Paroxysmal Anuria	\pm_1	\pm	\pm			0
Urticaria	-	-	-			0
Pulse rate	68	0	72			0
Sensibility to Cold	\pm	\pm	\pm			0
Tolerance to Treatment	\pm	\pm	\pm			0
Haemoglobin %	0	0	0			0
Knee Jerks	\pm	\pm	\pm			0
Pupil Re-action to light	\pm	\pm	\pm			0
Ascoli Test	0	0	0			0
Loss of weight	-	-	-			0
Gain in weight	-	-	-			0
Blood Pressure	120 S	110 S	108			0

Case No.	15.
Age	41
Sex	Female.
Occupation	Married. Multipara.
Causal Factor	Worry & Anxiety and Influenca.
Date of onset of symptoms	January 1925.
Date of commencing Treatment	May 1925.
Date of relinquishing Treatment	November 1925.
Result	In good health. December 1926.
Duration patient has been under observation	Six months.

H I S T O R Y:

This lady, who was abroad during the year 1924, had a most anxious time during November of that year, Her only son, aged 20 had a bad attack of Pneumonia, and the conditions under which he was attended were very bad.

She came home to England in December 1924, and gave me the following particulars about herself.

"She did not feel cold, her appetite was good, her bowels acted seven times a week, faeces were of proper consistency, and colour, and she

slept well, and di not know what it was to be depressed!"

Her husband, during this month developed Influenca, and she nursed him through it. In January, she herself had two mild attacks, but did not go to bed with either. It was after these attacks, that the symptoms began to come on. She was unable to walk $\frac{1}{2}$ mile without great fatigue. Her feet and hands were intensely cold. Her temperature was always sub-normal. She developed insomnia with bad dreams, and head aches. She became very constipated, her bowels only acting twice a week, they were very hard, and of a dark colour. She complained of an acute pain in her epigastrium, coming on between meals.

She went to Bournemouth, and was under treatment there two months, but was still the same when she returned. She saw a Specialist in Harley Street, and he advised a change and tonic, but unfortunately she did not improve.

I saw her in May 1925, and she was most depressed, crying several times during the consultation, and saying she was sure she was going to die. She was unable to walk at all, owing to extreme fatigue.

On Physical examination; lungs, nothing abnormal diagnosed; heart, very weak; pulse rate 68; Blood pressure 128 mm HG; Urine nil. tenderness marked in epigastrium, nothing else found.

She was put on Adreno Spermin Co, six tablets a day, and at once made rapid strides.

By the end of the month, she was able to walk one mile without fatigue, fits of depression were much alleviated, and she was sleeping much better.

Towards the end of July 1925, she was able to go to London with her Husband and to do a large amount of shopping in connection with the purchase of their new House.

She rather stupidly overdid things; going to Theatres, and Dances in the evening, and working hard at her business during the day, and when she came back, she had a relapse.

She was put on to the tablets six daily. (previous to going to London, she had got down to two daily) and again began to pick up, and within a month was quite well.

In December 1925, she was her former self, and went to Switzerland for the Winter Sports.

She is now able to walk six to seven miles without fatigue, no depression, her bowels acting every day, and are soft in consistency and proper colour. The pain has entirely gone, in fact, this pain left her within one month of the treatment and has never returned,

Case No.

XV.

Tabulated Symptoms.

Date	May 1925	Dec 1925	Dec 1926			
Muscular Asthenia	+ ₃	+ ₁	±			
Mental Asthenia	+ ₃	±	±			
Amount of Fatigue after slight exercise	+ ₃	+ ₁	+ ₁			
Constipation	+ ₃	±	±			
Insomnia	+ ₃	±	±			
Serjent's "White Adrenal Line"	+ ₁	±	+ ₁			
Dreams	+ ₃	+ ₁	+ ₁			
Pigmentation	0	—	—			
Paroxysmal Anuria	—	—	0			
Urticaria	+ ₂	—	+ ₁			
Pulse rate	68	74	68			
Sensibility to Cold	+ ₃	±	±			
Tolerance to Treatment	+	+	+			
Haemoglobin %	82%	88%	73%			
Knee Jerks	+	0	0			
Pupil Re-action to light	0	0	+			
Ascoli Test	0	+	+			
Loss of weight	+	—	±			
Gain in weight	—	+	±			
Blood Pressure	S. 128	S. 120	S. 124			

Case No.	16.
Age	63.
Sex	Female.
Occupation	Married. Multipara
Causal Factor	Tumour of Abdomen.
Date of onset of symptoms	1919.
Date of commencing Treatment	June 1922.
Date of relinquishing Treatment	August 1923
Result	Very great improvement for a time. Died September 1923.
Duration patient has been under observation	14 months.

H I S T O R Y:

Juandice (years ago.). She has never really enjoyed good health, having been the subject of bilious attacks for the greater portion of her life. This is also the case with her brothers and sisters. The bilious attacks occur almost weekly. Chronic constipation. Pyorrhoea. Influenca but only in mild forms.

December 1921. Four years ago, she was in her usual health, i.e. able to do her own housework and cooking, but very easily tired and always having recurring attacks of vomiting and pain in the right side of the abdomen. She has

gradually been getting very giddy.

The constipation is very marked, the bowels never acting unless strong purgatives are taken.

She complains of bronzing of the skin and very marked dyspnoea. Her appetite is failing she is unable to walk more than 1 mile. She also complains of a lump in her side. This lump was diagnosed by three Doctors as a cancerous growth.

February 1922. Getting gradually worse. Unable to walk. Bronzing more marked, vomiting becoming more persistent, loss of weight- three quarters of a stone in two months- Heart- endocarditis is present. Pain in epigastrium severe.

May 1922. Bed ridden. Bronzing very marked. Borborygmi were so loud, as to cause an unpleasant noise downstairs. Very constipated. Pulse rate 90. Systolic blood pressure 84 mm Hg. Further loss of weight. 'lump' very hard. sickness almost persistent.

14th June 1922. Seen by Mr C.E.S. Jackson F.R.C.S. and diagnosed:-

"Suffering from Cancer and unable to live until the end of the week." In fact she was moribund. In this I readily concurred.

15th June 1922. Sanitabs Adreno-Spermin Co begun, eight daily.

17th June 1922. Very marked improvement indeed. Sickness all stopped. Borborygmi only very occasionally, and then scarcely unpleasant. Pain much better. Able to keep Bengers food down.

20th June 1922. Very much stronger. Able to sit up in bed. Bowels acted without purgatives. This is the first time for years. Has had no vomiting or borborgymi. Wishes for food. Broth and eggs given, without vomiting. No pain but still very tired.

30th June 1922. Able to sit up in bedroom. Bowels acting without purges. The progress in my opinion, is astounding. Here we have what was a moribund woman on the 14th June 1922 actually sitting up in her bedroom on the 30th June- sixteen days after.

She has also been able to pass her bowels by herself. This too is a tremendous advance as it is years since she was able to do so without purges. The pain has also ceased.

26th July 1922. Still progressing. Has put on $\frac{1}{2}$ stone weight. Eats well. None of her unpleasant symptoms have returned. Bowels opened daily. Motions soft; they have ceased to be hard and like sheep droppings. She has been able to walk down the garden path

November 1922. Progress still being made. The asthenia was so much improved that she was able to go to the Village School $\frac{3}{4}$ mile away and record her vote at the General Election.

1923. During this year, she remained the same until the end of July when she began to develop oedema of ankles and legs, and also oedema of both bases of the lungs. The heart was dilated. She had to remain in bed and gradually sank; dying September 1923.

Right up to the time of her death, none of the cachectic symptoms returned. The bronzing always remained and during the whole time of the treatment, the blood pressure could not be got above 100 mm. HG.

It was the very great success in this case which led me to give the extracts a further trial. The effect of her "resurrection" as her daughter termed it, was very great to more than myself.

I was literally astounded by the rapidity with which the fatal symptoms one by one disappeared.

This was the first case I treated.

The Blood Pressure was extremely low, the systolic reading fell to 78 mm Hg.

June 1922. The case was moribund when treatment was begun. She had been seen by two Consultants who both agreed that she had "Cancer of the Bowel" and was in a cachectic state. She had been bedridden for six weeks, and was unable to raise herself.

July 1922. Benefit from Sanitabs Adreno-Spermin Co was immediate. Patient was able to get up and come downstairs with assistance. This shows the rapidity of action of the extracts even in extreme cases.

The lifelong constipation was overcome.

Although the patient died in a dropsical condition due to Valvular Disease of the Heart, she never again developed the 'cachectic symptoms'

She had a distinct tumour about the size of an orange situated to the right of the umbilicus.

She was never able to do without the Extract.

November 1922 Was able to go to the Parish School and vote at the General Election.

Case No.

XVI.

Tabulated Symptoms.

Date	June 1922	July 1922	Sept 1922	Dec 1922	June 1923	Sept 1923
Muscular Asthenia	+4	+2	+2	+2	+2	+2
Mental Asthenia	+3	+1	+1	+1	+1	+1
Amount of Fatigue after slight exercise	+4	+3	+2	+2	+2	+2
Constipation	+4	+2	±	±	±	±
Insomnia	+3	+1	+1	+1	+1	+1
Serjent's "White Adrenal Line"	—	—	—	—	—	—
Dreams	+1	+1	+1	+1	+1	+1
Pigmentation	+4	+3	+2	+2	+1	+1
Paroxysmal Anuria	+2	+1	+1	±	±	±
Urticaria	—	—	—	—	—	—
Pulse rate	90	94	92	88	86	90
Sensibility to Cold	+2	±	±	±	±	±
Tolerance to Treatment	+	+	+	+	+	+
Haemoglobin %	66%	68%	72%	70%	70%	68%
Knee Jerks	±	±	±	±	±	±
Pupil Re-action to light	+	+	+	+	+	+
Ascoli Test	0	0	0	0	0	0
Loss of weight	+3	+1	—	—	—	+1
Gain in weight	—	—	+1	±	+1	—
Blood Pressure	84	80	82	86	80	82

Case No.	17.
Age	67
Sex	Female.
Occupation	Married.Multipara.
Causal Factor	Shock.
Date of onset of symptoms	1922
Date of commencing Treatment	March 1925
Date of relinquishing Treatment	
Result	Continues in good health. December 1926.
Duration patient has been under observation	21 months.

H I S T O R Y:

Endocarditis, and more or less chronic bronchitis.

February 1925. Shock.

This patient, who has never been very strong, became very run down during the early part of 1925. She had had a very trying time during the winter of 1924, on account of her Husband's ill health; Following on this, she had a severe shock, her Husband dying suddenly whilst out motoring.

March 1925. She complained of being

depressed, inability to sleep, and a great amount of muscular fatigue.

Slight constipation all her life. Slight bronzing.

She was put on Adreno Spermin Co, three tablets a day, with the result that the insomnia was very much improved, and she was able to take a greater amount of muscular exercise than she had been able to do for the last few years.

Constipation and depression were both much improved, and she still continues to take the Adreno Spermin Co.

December 1925. Still improving.

December 1926. Has had a very good year.

Takes the tablets intermittently.

Case No.

XVII

Tabulated Symptoms.

Date	March 1925	July 1925	Dec 1925	Dec 1926		
Muscular Asthenia	+ ₂	+ ₁	+ ₁	+ ₁		
Mental Asthenia	+ ₁	±	±	±		
Amount of Fatigue after slight exercise	+ ₂	+ ₁	±	±		
Constipation	+ ₂	+ ₁	±	±		
Insomnia	+ ₂	±	±	±		
Serjent's "White Adrenal Line"	—	—	+	—		
Dreams	+ ₁	+ ₁	±	±		
Pigmentation	+ ₁	+ ₁	±	±		
Paroxysmal Anuria	—	—	—	—		
Urticaria	—	—	—	—		
Pulse rate	78	72	68	76		
Sensibility to Cold	+ ₁	+ ₁	±	±		
Tolerance to Treatment	+	+	+	+		
Haemoglobin %	0	0	0	0		
Knee Jerks	+	0	0	0		
Pupil Re-action to light	0	0	0	0		
Ascoli Test	0	0	0	+		
Loss of weight	+	+	+	+		
Gain in weight	—	±	±	+		
Blood Pressure	0	0	0	0		

Case No.	18.
Age	36
Sex	Female.
Occupation	Married. No Children
Causal Factor	?
Date of onset of symptoms	years
Date of commencing Treatment	May 1924.
Date of relinquishing Treatment	July 1924.
Result	Had a definite reaction to Adreno Spermin Co.
Duration patient has been under observation	2½ years.

H I S T O R Y:

This patient has been suffering from nerves for the past seven years. She complains of an acute pain over the region of her gall bladder and pain across the lower part of her back.

Her nervous symptoms are as follows:- Very depressed, worries greatly about small things, has bad dreams, is unable to concentrate. She does not feel able to work and is very tired. especially after muscular fatigue. She is passing large quantities of water daily.

Borborygmi are marked. She suffers from constipation, and the faeces are very hard. She complains lately of the cold, and has had an urticarial eruption.

On Physical examination a Bismuth meal revealed a general Gastroph~~it~~osis.

Heart & Lungs, nothing abnormal diagnosed. Pulse rate 84. Blood pressure 180 mm Hg. Temperature sub-normal.

I first saw this patient in 1925, and at that times she was complaining of sick head aches and sickness with her periods. I advised Hormotones which is chiefly Ovarian Extract. She has been taking these continuously until now, and is almost entirely cured of her sick headaches.

For the Gastroph~~it~~osis she wears a belt. I hoped from the general outline of her symptoms that Adreno Spermin Co would have benefitted them, and accordingly ordered her to take 4 tablets a day. Within a fortnight she was not so well, and by the ened of the month, was very much worse, so the treatment was discontinued, and the Hormotones re-ordered. On seeing her two weeks later, the Hormotones had picked her up.

She has an interesting symptom, which is worth noticing.viz: Although normally constipated she has, what almost amounts to diahorrea during her periods.

Case No.

XVIII

Tabulated Symptoms.

Date	4 MAY, 1924.	18 MAY, 1924.	JUNE 1925.			
Muscular Asthenia	+ ₁	+ ₁	+ ₁			
Mental Asthenia	+ ₃	+ ₃	+ ₃			
Amount of Fatigue after slight exercise	+ ₁	+ ₁	± ₁			
Constipation	+ ₃	+ ₃	+ ₃			
Insomnia	+ ₂	+ ₂	+ ₃			
Serjent's "White Adrenal Line"	+	+	+			
Dreams	+ ₂	+ ₂	±			
Pigmentation	-	-	-			
Paroxysmal Anuria	-	-	-			
Urticaria	+ ₁	+ ₁	+ ₁			
Pulse rate	84	88	74.			
Sensibility to Cold	+ ₂	+ ₂	+ ₂			
Tolerance to Treatment	- ₂	-	-			
Haemoglobin %	0	0	0			
Knee Jerks	0	0	0			
Pupil Re-action to light	+	+	+			
Ascoli Test	+	+	+			
Loss of weight	+	±	±			
Gain in weight	+	±	+			
Blood Pressure	5180 90	5182 110	5164 98			

Case No.	19
Age	38
Sex	Male.
Occupation	Medical Practitioner
Causal Factor	Worry
Date of onset of symptoms	May 1925.
Date of commencing Treatment	July 1925
Date of relinquishing Treatment	
Result	Cured. December 1926.
Duration patient has been under observation:-	18 months.

H I S T O R Y:

January 1925. Concussion.

This patient was a personal Medical friend with whom I was staying, and he appeared to me to be depressed. I asked him about himself in a casual way, and he stated that he was feeling 'down'. He had just bought a new Practice and disliked the neighbourhood (viz. The Fens), and he disliked the people, and he had no vim for work. I was struck by this, as he had been a very very keen worker during the previous ten years.

He seemed to think that it would be necessary for him to sell his practice, and get out of it all. He was not sleeping well, and had no appetite. I told him of the Adreno-Spermin Co., tablets, and the success I had had in my practice and advised him to try it himself. This, he did, and he wrote me a letter three weeks later, saying that he felt an entirely different man, and was seeing 'life' through another pair of spectacles.

He did not know whether to attribute this to the Adreno-Spermin Co., which he had been taking or to a brighter financial out-look, his affairs having greatly improved. (He had no financial worries).

Case No. ~~XXX~~

Tabulated Symptoms.

Date	July 1925	Aug 1925				
Muscular Asthenia	+	+				
Mental Asthenia	+3	+				
Amount of Fatigue after slight exercise	+	+				
Constipation	+	+				
Insomnia	+2	+				
Serjent's "White Adrenal Line"	0	0				
Dreams	0	0				
Pigmentation	0	0				
Paroxysmal Anuria	0	0				
Urticaria	0	0				
Pulse rate	0	0				
Sensibility to Cold	0	0				
Tolerance to Treatment	+	+				
Haemoglobin %	0	0				
Knee Jerks	0	0				
Pupil Re-action to light	0	0				
Ascoli Test	0	0				
Loss of weight	0	0				
Gain in weight	0	0				
Blood Pressure	0	0				

Case No.	20.
Age	34
Sex	Female.
Occupation	Married Multipara
Causal Factor	Worry
Date of onset of symptoms	Beginning of 1925.
Date of commencing Treatment	October 1925.
Date of relinquishing Treatment	December 1925.
Result	Improved.
Duration patient has been under observation	three months.

H I S T O R Y:

October 9th 1925. This patient complained of being unable to sleep. Restlessness when asleep. Goes to bed at 9 and sleeps until 11.P.M. and then restless. 'When waking in the morning has a load of trouble' Little things worry her. She becomes very depressed two or three times weekly, and lasting all day.

Backaches on walking. Headaches at the back of the head- hot flushes.

This week, troubled with wind. Bowels opened daily, some days alright, and then constipated

Case No.	20.
Age	34
Sex	Female.
Occupation	Married Multipara
Causal Factor	Worry
Date of onset of symptoms	Beginning of 1925.
Date of commencing Treatment	October 1925.
Date of relinquishing Treatment	December 1925.
Result	Improved.
Duration patient has been under observation	three months.

H I S T O R Y:

October 9th 1925. This patient complained of being unable to sleep. Restlessness when asleep. Goes to bed at 9 and sleeps until 11. P.M. and then restless. 'When waking in the morning has a load of trouble' Little things worry her. She becomes very depressed two or three times weekly, and lasting all day.

Backaches on walking. Headaches at the back of the head- hot flushes.

This week, troubled with wind. Bowels opened daily, some days alright, and then constipated for a day or two, like cinders.

Occasionally painful to defaecate. Unable to walk a mile without great fatigue. Appetite bad. Bowels a very dark oak colour. Feels the cold xxx Has red patches on the back and chest occasionally.

Discharge from vagina xx. Urine xx and then - -. Blood Pressure 118 mm Hg.

Had influenza for a week in March 1925, and took a long time to recover.

December 1925, Getting improvement from the treatment, but has now given it up on account of expense, I think.

December 1926. Has been lost trace of.

Case No. XX. Tabulated Symptoms.

Date	Oct. 1925	Dec. 1925				
Muscular Asthenia	+ ₂	+ ₁				
Mental Asthenia	+ ₁	±				
Amount of Fatigue after slight exercise	+ ₃	+ ₁				
Constipation	+ ₂	+ ₁				
Insomnia	+ ₂	±				
Serjent's "White Adrenal Line"	+	—				
Dreams	+ ₂	+ ₁				
Pigmentation	0	0				
Paroxysmal Anuria	+ ₁	±				
Urticaria	+ ₁	±				
Pulse rate	78	82				
Sensibility to Cold	+ ₃	+ ₂				
Tolerance to Treatment	+	+				
Haemoglobin %	0	0				
Knee Jerks	0	0				
Pupil Re-action to light	0	0				
Ascoli Test	—	0				
Loss of weight	±	±				
Gain in weight	±	±				
Blood Pressure	5.118	0				

Case No.	21.
Age	58
Sex	Male.
Occupation	Medical Officer.
Causal Factor	Worry
Date of onset of symptoms	November 8th 1925.
Date of commencing Treatment	November 17th 1925
Date of relinquishing Treatment	November 24th 1925.
Result	Cured.
Duration patient has been under observation	One month.

H I S T O R Y:

1923. This is a case of another personal friend. During the year of 1923, he had a very great deal of worry. His wife undergoing a very serious operation, which has left her a semi-invalid.

October 1925. She had to leave him to nurse her Father who was dying. These family worries together with over-work had been telling on him until November 8th when he completely crocked up.

He was suffering from complete mental apathy, and inability to take a job.

He was very constipated, a symptom, which was foreign to him, very depressed, he had no appetite whatsoever, and carried on with his work as well as he could, with one or two cups of tea a day.

He had been taking Eastern Syrup and Bromides at night to make him sleep.

When I saw him, I advised him to take Adreno Spermin Co 5 tablets daily, and at the end of the first day, he rang me up on the telephone to say that he felt much better, and that night he slept well, and by the end of a week, he stopped taking the Adreno Spermin Co, as he felt so much better, and was able to continue his work quite easily.

Case No. XXI

Tabulated Symptoms.

Date	Nov. 1925	Dec. 1925				
Muscular Asthenia	+ ₃	±				
Mental Asthenia	+ ₃	±				
Amount of Fatigue after slight exercise	+ ₃	±				
Constipation	+ ₂	±				
Insomnia	+ ₃	±				
Serjent's "White Adrenal Line"	—	+				
Dreams	—	—				
Pigmentation	—	—				
Paroxysmal Anuria	—	—				
Urticaria	—	—				
Pulse rate	88	84				
Sensibility to Cold	±	±				
Tolerance to Treatment	+	+				
Haemoglobin %	0	0				
Knee Jerks	±	±				
Pupil Re-action to light	0	0				
Ascoli Test	—	—				
Loss of weight	±	±				
Gain in weight	±	±				
Blood Pressure	+	+				

Case No.	22.
Age	38
Sex	Female.
Occupation	Married. Multipara
Causal Factor	Influenza. 1924.
Date of onset of symptoms	December 1924.
Date of commencing Treatment	February 1925.
Date of relinquishing Treatment	March 1925.
Result	Cured. December 1926
Duration patient has been under observation	21. months,

H I S T O R Y:

February 1925. This patient had a bad attack of Influenza in 1924, and she was left with the following symptoms:-

Muscular fatigue, insomnia, depression, worry. She was very nervous that she had an abdominal tumour which would require an operation. Rather constipated, and short of breath. She had been in this condition two or three months, when she came to me, and had been under treatment all this time, and had not got any better .

On physical examination, nothing abnormal was found.

Pulse rate 80. Blood pressure 130mm Hg. She did not show Sargent's Line.

I assured her that she had no abdominal tumour and prescribed Adreno Spermin Co. She remained under my Care for a month, during which time she became perfectly well, and returned home. (March 1925.)

December 1925. I heard from her the other day, and she said she was perfectly well and had no relapse of her symptoms.

Case No. XXII

Tabulated Symptoms.

Date	Feb. 1925.	Mar. 1925.	Dec. 1925.			
Muscular Asthenia	+ ₂	±	±			
Mental Asthenia	+ ₂	±	±			
Amount of Fatigue after slight exercise	+ ₃	±	±			
Constipation	+ ₁	±	±			
Insomnia	+ ₂	±	±			
Serjent's "White Adrenal Line"	—	+	0			
Dreams	—	—	0			
Pigmentation	—	—	0			
Paroxysmal Anuria	—	—	—			
Urticaria	—	—	0			
Pulse rate	80	82	76			
Sensibility to Cold	±	±	0			
Tolerance to Treatment	+	+	±			
Haemoglobin %	84%	80%	88%			
Knee Jerks	+	0	±			
Pupil Re-action to light	+	0	0			
Ascoli Test	0	0	0			
Loss of weight	±	±	0			
Gain in weight	±	±	0			
Blood Pressure	130.5 66.8	124.5 70.8	0			

Case No.	23.
Age	37
Sex	Female.
Occupation	Married. Multipara
Causal Factor	Shock.
Date of onset of symptoms	1919
Date of commencing Treatment	Oct. 20th 1925.
Date of relinquishing Treatment	
Result	
Duration patient has been under observation	

H I S T O R Y:

Shock. Until the year 1919, she was a strong healthy young woman, but at that date, she was fool-hardy enough to allow a dentist to extract 26 teeth at one sitting, and after this, she completely lost her nerve. Previous to this, she did not know what nerves were.

She was afraid to go out in the dark, and was very depressed. Since that date, she has had days of inability to do anything, and feels that everything is too much bother for her. She has slept well, until lately, when she awakes at

midnight and is unable to sleep again.

She had bad dreams. Since the extraction of her teeth, she is subject to nettle rash.

She is constipated, the faeces being hard, and large lumps and very dark.

She has always been subject to fainting attacks, three or four coming on each month, These attacks are usually brought on by viewing something unpleasant.

May 1925. These symptoms were brought to a head by her son having an acute appendicitis, which necessitated his removal to Hospital. At this time, she was confined to her room for a fortnight and she was very depressed and worried.

Two months later, these symptoms were again severely agitated by a severe fright. She was cycling along a road, when a man tried to stop her, and then kept following her for several miles.

Owing to constipation, she was suffering from Piles, and was rather worried about their removal.

October 15th 1925. On this date, she was operated on and the Haemorrhoids removed.

Immediately after the operation, I gave her Adreno Spermin Co and by the 2nd November 1925, she reports she is improved. She is sleeping better her Blood pressure is the same as it was before the operation, 145 mm Hg.

By the end of November, her pulse rate was

88, and she reports she is very much better.

Her bowels are acting ten times a week, and were soft. Sleep was better, and for the past week had had no dreams at all.

Depression gone, and no fainting attacks, since the commencement of Adreno Spermin Co . She still complains of pain in her back.

She has ceased to worry and looks, and is, an entirely different person.

December 7th 1925. She reports that she has had no fainting attacks, and feels she has done with them for ever. She sleeps well, and although having had some dreams this week, they were not terrifying. Bowels open every day and quite soft. Back ache a little better.

December 1926. Has kept well all this year, and has discontinued treatment.

Case No.

XXIII

Tabulated Symptoms.

Date	May 1925	July 1925	Dec 1925	Dec 1926		
Muscular Asthenia	+ ₃	+ ₁	±	±		
Mental Asthenia	+ ₃	±	±	±		
Amount of Fatigue after slight exercise	+ ₂	+ ₁	±	±		
Constipation	+ ₃	+ ₁	±	±		
Insomnia	+ ₂	±	±	±		
Serjent's "White Adrenal Line"	+	+	+	+		
Dreams	+ ₃	+ ₁	±	±		
Pigmentation	—	—	—	—		
Paroxysmal Anuria	—	—	—	—		
Urticaria	+ ₁	±	±	±		
Pulse rate	80	84	74	76		
Sensibility to Cold	+ ₁	±	±	±		
Tolerance to Treatment	+	+	+	+		
Haemoglobin %	0	0	0	0		
Knee Jerks	+	0	0	0		
Pupil Re-action to light	+	0	0	0		
Ascoli Test	+ ₁	+ ₁	+ ₂	+ ₁		
Loss of weight	—	—	—	—		
Gain in weight	—	—	—	—		
Blood Pressure	145.5	S. 142 D. 80	S. 160 D. 92	S 134 0		

Case No.	25.
Age	45
Sex	Female.
Occupation	Married. no children
Causal Factor	Mental worry. dread of cancer.
Date of onset of symptoms	October 1925.
Date of commencing Treatment	November 9th 1925
Date of relinquishing Treatment	December 1925.
Result	Cured. December 1926.
Duration patient has been under observation	14 months.

H I S T O R Y:

November 9th 1925. The patient has been ill for the past three weeks; she has had a complete 'nervous breakdown', Acute depression set in. She had been suffering from Insomnia for the past year; sleeping four hours a night, sleep being broken by bad dreams. Constipation for past three or four years. Bowels only acting three times a week

Pain in pre cordia coming on after food (within half an hour) No heartburn.

Very short of breath.

She is very tired after walking a mile.

November 13th.1925. The urine is not being passed so frequently atnight. Patient states that within one day of taking tablets she "lost her depression and that heavy feeling" Her friends remarked that they had never seen so quick a change in anyone.

December 1925. Is now her normal self. The bowels act normally. Sleep is very much improved. All fear of cancer has disappeared.

Treatment discontinued.

December 1926. Has had an normal year.

Case No. XXV

Tabulated Symptoms.

Date	Nov 9th 1925	Dec 1925				
Muscular Asthenia	+ ₂	+				
Mental Asthenia	+ ₂	+				
Amount of Fatigue after slight exercise	+ ₃	+				
Constipation	+ ₃	+ ₁				
Insomnia	+ ₂	+				
Serjent's "White Adrenal Line"	+ ₂	+ ₂				
Dreams	+ ₂	±				
Pigmentation	0	0				
Paroxysmal ^{Polyuria} Anuria	+	-				
Urticaria	-	-				
Pulse rate	72	68				
Sensibility to Cold	+ ₁	+				
Tolerance to Treatment	+	+				
Haemoglobin %	0	0				
Knee Jerks	+	0				
Pupil Re-action to light	0	0				
Ascoli Test	-	-				
Loss of weight	+ ₂	±				
Gain in weight	-	±				
Blood Pressure	5/80	5/68				

Case No.	27.
Age	36
Sex	Male.
Occupation	Male.
Causal Factor	Influenca.
Date of onset of symptoms	6th September 1925
Date of commencing Treatment	20th September 1925
Date of relinquishing Treatment	October 1925.
Result	Cured. December 1926
Duration patient has been under observation	six months.

H I S T O R Y:

This is also a case of a personal friend of mine. He had a very bad attack of influenza which left him very weak and very tired, he could hardly be bothered to read the newspapers, and it was perfect agony to write a letter to his Mother.

No constipation, slept fairly well, but was troubled with bad dreams.

Chief symptom was mental apathy.

He stated that physically he could work, but mentally he could not.

On Physical examination, nothing abnormal was found, except a slow pulse. 68. Blood pressure 125 mm Hg.

Bowels were acting daily. He had tried to pick himself up with Syrup Glycerophosphates but this had no effect.

I advised him to try Adreno Spermin Co, which he did, and at the end of a fortnight's treatment, he informed me that it began to act well the moment he started taking the treatment, and he is feeling quite fit.

Case No.	28.
Age	45.
Sex	Female.
Occupation	Married to a Publican
Causal Factor	Worry & Overwork.
Date of onset of symptoms	November 1925.
Date of commencing Treatment	November 1925.
Date of relinquishing Treatment	December 1925.
Result	Cured. December 1925
Duration patient has been under observation	One month

H I S T O R Y:

October 1925. Had a great deal of anxiety with regard to her daughter's lover affairs, and also had a very great deal of work to do.

November 6th 1925. She consulted me, and complained of being very tired and having occasional attacks of acute depression. As she had been a mental Nurse, these fits of depression together with the cessation of her menses worried her considerably; she was afraid of "melancholia" She was sleeping badly. No appetite, Bowels only acting four times a week, and rather hard. She

has had very bad dreams for the past two weeks, although she is not in the habit of dreaming.

During the past six months has had slight urticarial eruptions; on two occasions, she only passed a small quantity of urine each day for three days, she only passed ~~six~~ ounces of urine in 72 hours. She has no appetite.

The patient became very depressed when she was speaking to me, and began to cry, and at the same time telling me she could not help it.

Treatment with Adreno Spermin Co was commenced.

November 10th 1925. Has been "ever so well for the past three days"

November 16th 1925. Improvement still maintained, has had one or two fits of depression. They have not been so severe, and are at once controlled by a "Tablet". In fact she has been so much better that she only takes one tablet a day now. Bowels acted every day last week. and were much softer.

November 30th 1925. Has still improved, and had no fits of depression. Feels quite herself again. Sleeping well, appetite very good.

Treatment to be continued for another fortnight.

December 1925. Very well. Treatment discontinued.

December 1926. Has had a very good year in spite of many mental worries.

No period since July 1924.

The effects of the treatment were felt within 20 minutes of taking the first tablet.

She only took three a day for two days because she felt so much better, she started taking one a day, which kept her very well.

A fit of depression and nerves is at once cured by a Tablet.

Case No. xxvii

Tabulated Symptoms.

Date	Nov 1925	Dec 1925				
Muscular Asthenia	+ ₁	+ ₁				
Mental Asthenia	+ ₃	+ ₁				
Amount of Fatigue after slight exercise	+ ₂	+ ₁				
Constipation	+ ₂	±				
Insomnia	+ ₂	±				
Serjent's "White Adrenal Line"	+ ₁	+ ₁				
Dreams	+ ₁	±				
Pigmentation	-	-				
Paroxysmal Anuria	+ ₁	±				
Urticaria	+ ₁	±				
Pulse rate	88	92				
Sensibility to Cold	+ ₂	+ ₂				
Tolerance to Treatment	+	+				
Haemoglobin %	90%	84%				
Knee Jerks	+	0				
Pupil Re-action to light	+	0				
Ascoli Test	+	+				
Loss of weight	±	±				
Gain in weight	±	±				
Blood Pressure	148.	134.				

Case No.	29.
Age	27
Sex	Female.
Occupation	School Teacher.
Causal Factor	Unknown
Date of onset of symptoms	1919
Date of commencing Treatment	August 1924.
Date of relinquishing Treatment	March 1925.
Result	Cured.
Duration patient has been under observation	$1\frac{1}{2}$ years

H I S T O R Y:

This lady was healthy in every respect, except that she suffered from Headaches, which seemed to be much worse before her Menstrual period. She also complained of being rather nervy. At times she had slight depression.

The bowels acted every day. She slept fairly well- no dreams. Passed the normal quantity of urine.

Blood pressure 115 mm Hg Pulse 76. Nothing abnormal was found. She really consulted me on account of her head aches. I thought that these

head aches had an Endocrine origin and I tried Ovarian Extract. This did little good. I therefore tried Adreno Spermin Co and advised her to take three tablets per day for a fortnight before every period.

She now reports that there is a perfect cure. I am not certain if the Thyroid might not have been equally successful.

Case No.	30.
Age	54
Sex	Female.
Occupation	Nil.
Causal Factor	Unknown.
Date of onset of symptoms	July 1921.
Date of commencing Treatment	1924.
Date of relinquishing Treatment	
Result	Cured.
Duration patient has been under observation	Six months.

H I S T O R Y:

1916. Appendix removed in Paris.

She complains of nervy exhaustion; flatulence
Pain over pre cordia. She eats well : her bowels
are relaxed: She sleeps fairly well, but she
goes about with the eternal dread of having an
abdominal tumour. This causes an acute depression

On Physical examination. P.V. and P.R.
nothing abnormal . Her urine showed no trace
of albumen. Muscular fatigue was present.

August 1924. Adreno Spermin Co given four
tablets daily.

December 1924. I saw her again, and she

states she is very much improved, and
attributes this to the taking of the tablets.

Case No. 31.

Age 22.

Sex Female.

Occupation Social Welfare Worker.

Causal Factor Worry.

Date of onset of symptoms October 1922.

Date of commencing Treatment April 1923.

Date of relinquishing Treatment June 1923.

Result

Duration patient has been under observation
1½ years

H I S T O R Y:

April 1923. Complains of weakness: breathlessness and general fatigue: Chiefly mental fatigue. Her work has become so heavy that she had to discontinue it, because she was unable to cope with it. She has been under treatment for three months in Yorkshire, and has been sent away for six months rest with her Norfolk friends.

It is now four months since her rest commenced and she is still no better. Her inability to do things seems to be an obsession.

*
On Physical examination, heart and lungs

negative. She is very nervous.

Constipation is present. Cold hands and feet. Her blood pressure is 100 mm Hg. Urine- nothing abnormal diagnosed. Menstruation scant and painful.

Tablets Adreno Spermin Co five daily were ordered. In a fortnight, she reports she feels very much better.

Returns to work in six weeks, and to quote her own opinion:- "I am perfectly well".

I have not seen her since January 1924, but heard indirectly in October 1924, that she was still at work, and perfectly well.

Case No.	32.
Age	39
Sex	Female.
Occupation	Independent.
Causal Factor	Hereditary probably.
Date of onset of symptoms	All her life.
Date of commencing Treatment	February 1923.
Date of relinquishing Treatment	
Result	Cured whilst taking tablets
Duration patient has been under observation	2½ years.

H I S T O R Y:

Gives a History of 'Delicacy', without any definite complaint. Her mother says she possesses no energy to do anything, and has no reserve of strenght. She is of a worrying and an xious nature, subject to nervy storms. Loses weight quickly and complains of mental anxiety. She also complains of constipation and feeling cold. Palpitation and a lot of pre-menstrual pains.

Blood pressure 105 mm Hg.

On Physical examination, heart and lungs,
Nothing abnormal diagnosed. Urine nil:

This patient was rather difficult to
investigate, she continually broke down and
cried.

Tablets Adreno Spermin Co were given and in
two weeks there was a vast improvement. All
her symptoms had assumed smaller proportions.

March 1923. She reports, 'Better than I
have ever been before'

October 1925. The Patient's condition to
date keeps well so long as she remains on
her tablets. She cannot leave off these
without a relapse.

Case No. 33.
Age 53
Sex Female.
Occupation Nurse.
Casual Factor.
Date of onset of symptoms. Gradually from 1917.
Date of commencing Treatment May 1923.
Date of relinquishing Treatment.
Result
Duration patient was under observation.
two years.

H I S T O R Y.

1917. Gastrophthosis, for which she wore a Curtis Belt.

This patient has been a Maternity Nurse for the past 20 years. She has been working particularly hard during the past two years, and has not been feeling herself.

Her symptoms have gradually been getting worse. She complains of being run down, insomnia, pain, and irritation round the Pulva and anus. She is nervous and afraid of the dark, and she fears she had a growth.

The wearing of the Curtis Belt caused pressure on the kidneys with frequent micturition, but with a diminution of the quantity of urine.

On Physical examination her lungs were normal. Abdominal walls flacid,

P V. and P.R. considerable tenderness and inflammation. Urine , no sugar and nothing abnormal found.

Menstruation ceased 12 years ago.

May 1923. Treatment ordered was Adreno Spermin Co. 5 tablets daily. She was assured that there was no growth present.

Alkaline douches were given for the irritation and pain. In one month this patient reported that all her symptoms had disappeared and work had again become a pleasure.

The blood pressure at the end of one month was 150 mm Hg. Treatment was then discontinued.

September 1923. This patient had a relapse the chief complaint being, sleeplessness, and muscular weakness. Pain on both sides of spine in the Dorsal and lumbar regions.

On account of expense, Thyroid tablets were prescribed. The result was as good, and the Nurse is still working away on full duty. She states that the Thyroid tablets do not give her the same mental relief as the Adreno Spermin Co, but they they have relieved her pain and helped her to sleep.

Case No. 34
Age. 36
Sex. Female.
Occupation Independent.
Casual Factor.
Date of onset of symptoms. 1918.
Date of commencing Treatment November 1922
Date of relinquishing treatment. February 1923
Result. Cured.
Duration patient ~~has~~ been under
observation
four months.

H I S T O R Y.

Complains of tiredness especially after exercise. Palpitation and constipation.

On Physical examination her heart and lungs nothing abnormal found. Blood pressure was taken. Urine clear.

Rest in bed advised and a mixture containing Digitalis was given. Result. no improvement.

Eastern Syrup gave her gastritis, and had to be discontinued.

The patient having had a long rest in bed

still complains of weakness and especially
mental fatigue

Adreno Spermin Co tablets three a day
were started.

By February 1923, she was very well
indeed and went travelling on the Continent.

Case No. 35.
Age. 40.
Sex. Female.
Occupation Married.
Casual Factor.
Date of onset of symptoms. 1914.
Date of Commencing Treatment.
Date of relinquishing Treatment.
Result.
Duration patient has been under observation.

H I S T O R Y.

She complains of pain in her back, and says her chief complaints are depression, muscular weakness, and fatigue. She has suffered from these for the past ten years. She is sleepless Only obtaining two hours sleep each night. Her sleep is troubled with bad dreams. She is very constipated, her bowels only acting two or three times a week.

On Physical examination, she was very thin emaciated, and anxious looking. P.V. Uterus acutely retroflexed. Sluffing of the Os and acute vaginal discharge. Hysterectomy advised

and refused.

Treatment. Ulcer iodised twice weekly, and Adreno Spermin Co given. After one month's treatment, the ulcer was healed and the discharge very much improved, and the depression very much better.

She is now able to wear a ring pessary.

At the end of six months (during which time she had been taking Adreno Spermin Co) the treatment was discontinued owing to expense. The ulcer returned , pain in back, and vaginal discharge. These symptoms continued and I ultimately advised her to have an operation in June 1924.

After the operation, the patient felt very much better and although she still has occasional attacks of depression these are easily dispelled by a short course of the Adreno Spermin Co tablets.

Case No.	36
Age	36
Sex.	Female.
Occupation.	Married.
Casual Factor.	
Date of onset of symptoms.	January 1923.
Date of commencing treatment.	October 1923.
Date of relinquishing Treatment.	April 1924
Result.	Very much improved.
Duration of patient has been under observation.	2 years 9 months

H I S T O R Y.

October 1923. She complained of vaginal discharge, weakness pain in back. Mental depression, Feels the cold acutely, and is losing weight. She refuses vaginal examination as fears an operation may be required, and only wishes me to treat her with medicines.

She suffers from constipation, bowels only acting two or three times a week. She is particularly nervous and frightened.

Physical examination of the heart and lungs

nothing abnormal found.

Blood pressure 110 mm Hg.

Tablets Adreno Spermin Co, five daily commenced.

November 1923. In one month her general condition vry much improved. The blood pressure rising to 120 mm Hg, the patient was very much better in every way.

Vaginal discharge was profuse, but at this consultation she consented to an examination and an ulcer of the servex was found. This ulcer was healed after eight weeks bi-weekly treatment with iodine.

She is now taking her tablets one month in three and is well, and fat and carrying on with her usual games and enjoying her work

AN ANALYSIS OF THE SYMPTOMS.

	[%] Incidence	% Relieved by Treatment.
Depression	98%	98%
Muscular Fatigue	98%	96%
Mental Apathy	75%	92%
Constipation	75%	92%
Insomnia	75%	92%
Sargents Line	50%	50%
Dreams	60%	88%
Low Blood Pressure	33 $\frac{1}{3}$ %	42%
Anuria	25%	100%
Pigmentation	9%	31%

From these figures it will be at once seen that the effect of treatment is most marked on the purely subjective symptoms.

That it had practically no effect on Pigmentation.

That it had quite a small degree of effect on "Sargents White Adrenal Line", and a still lesser effect on the blood pressure.

The disease appears to be relatively twice as common amongst women than men.

SUMMARY OF 27 CASES.

N.B. Cases 28-35 are not included in the summary.
These case records were kindly lent to me by Dr
Mary Poole of Norwich.

The cause of the asthenic symptom complex
was:-

Functional	in	88%)	Influenza 22.2%
)	Worry, Shock &c. 37%
Organic	in	12%		
Females	in	66.6%		
Males	in	33.4%		

The results of the Treatment:

Cured and treatment ceased	40.7%
Cured but treatment must be continued	33.3%
Improved but treatment " " "	14.2%
Improved temporarily, but have died.	7.4%
No benefit	7.4%

SUMMARY.

A resume of the history of the Supra Renal gland appears to leave two definite facts well established. The first of these, is perhaps the more remarkable because it was almost the first discovery of note with relation to this gland; viz that the Addisonian syndrome is due to disease of the Supra renal gland or the chromophil tissue of the body. The second and the more important is that the Cortex is essential to life, and that there is not sufficient evidence to show that the medulla is absolutely essential to life.

It is acknowledged by all authorities that Addison's disease is a most insidious one. The asthenia comes on very slowly and it is often accompanied by fits of depression and irritability

Gastric disturbances are also present and the chief of these is constipation. The blood pressure ⁱⁿ ~~is~~ this early stage begins to fall.

The above are the typical symptoms, of the onset of Addisons' Disease.

With the appearance of pigmentation, and in all such cases brought to Autopsy, the Supra Renal Gland has been found to be diseased, the diagnosis is confirmed.

There have been many cases where the pigmentation has been entirely absent, and yet the case has been due to disease of the supra renal gland. On the other hand the pigmentation may be very deep and the other symptoms relatively slight. It would therefore appear that the Asthenia and the pigmentation do not have the same pathological foundation.

Physiologists have been able to reproduce the Asthenic condition in animals, but so far they have been quite unable to reproduce the 'pigmentation'.

At what stage does the dysfunction of the gland commence.

In the absence of any other sufficient clinical cause it is reasonable to assume that the onset of the Asthenia is the outward and clinical sign that the supra renal gland is commencing to fail in its function. If this is so and the disease of the gland is progressive the typical Addisonian picture will be reproduced.

There is however no data on which we must assume that the diseases of the Supra Renal Gland must in every case be severe and progressive.

There is no reason why disease of the gland may not be arrested at any stage in its course. or that there may even be a functional disorganization of the gland without any actual organic lesion .

What then are the early symptoms of dysfunction of the Supra Renal Glands?

They should approximate very closely to the primary symptoms of Addison's Disease, e.g. Mental and Muscular asthenia with constipation and a low blood pressure should be constant symptoms.

That the above symptom complex occurs with startling frequency will be admitted by almost everyone. It occurs very frequently by itself and apparently is due in these cases to an overstraining of the tissue. It is a frequent sequelae to Influenza and to all the infectious diseases more especially after diphtheria. In this case, there is some evidence that the Diphtheria toxin has a selective action on the Supra Renal Gland. There is a great mass of pathological proof that Influenza has also a specific effect on the supra renal gland. In both of these conditions the clinical picture shows a marked degree of asthenia. It has been shown that fear and pain cause a distinct re-action from the medulla of the supra renal.

The above symptom complex is witnessed in all degrees after a severe mental shock or fright.

It has been definitely proved on animals that the cortex is essential to life.

It is therefore reasonable to assume that a slight dysfunction of so small amount of tissue which is absolutely essential to life, must be demonstrated by some clinical sign.

There is abundant evidence to show that the medulla plays a very important part in the functions of the Human Body, and therefore it too must have clinical manifestations for its dysfunctions.

In this case, we have a very complete knowledge of the functions of Adrenaline which is an active secretion given out by the medulla. These functions are the same as the results obtained by stimulating the sympathetic nervous system. Therefore ~~is~~ there is less adrenaline given out from the medulla than normal, there should be clinical signs which should be the opposite effects to those obtained by stimulation of the sympathetic and these would be a fall in temperature, a lowering of blood pressure, and an excitation of the tone of the small intestines and of the spontaneous rhythm of the muscular walls, a weakened hearts' action, a slowing of the respiratory rate and contraction of the pupils, and we should expect these clinical symptoms to appear in a case of dysfunction in the supra renal gland.

In Addison's Disease we see all these clinical signs. The increased tonus of the small intestines is probably responsible for the spastic constipation.

The skin is dry, the heart's action is weak, the respirations are slow and shallow. The temperature and the Blood Pressure are subnormal.

It is therefore evident whatever the connection between the two facts may be, that some of the signs and symptoms of Addison's Disease are identical with the effects we should expect to obtain if the sympathetic nervous system were all depressed, and that these signs and symptoms are directly antagonistic to the physiological actions of adrenaline.

The symptom complex which I have described is identical with the earlier symptoms of Addison's disease and this symptom Complex in its severer forms becomes more and more like a true Addison manifestation until the pigmentation appears and it is clinically permitted to diagnose the major condition. The symptoms of the two conditions are identical; today we have the complete symptom Complex resembling Addison's Disease, but without pigmentation, tomorrow the pigmentation appears and we have Addison's Disease. Surely it is stretching scientific agnosticism too far to suggest that in the former there is no involvement of the supra renal gland and in the latter the gland is extensively destroyed.

We are therefore forced to the conclusion that there can be disease of the Supra Renal gland without pigmentation, and that this disease gives definite symptoms which are identical with the early

symptoms of Addison's Disease.

In the twenty eight cases which have been recorded, each one showed this definite chain of symptoms. Twentysix showed a very definite and beneficial re-action to the following specific line of treatment.

Rx.
Adrenal Substance(total) gr $\frac{1}{4}$
Thyroid Gland.(U.S.P. ix) gr $\frac{1}{2}$
Spermin Extract from gonads gr 2
Calcium Glycerophosphate q.s.
ad gr. 5.

Sig. Fiate the Tablet.

One to six daily immediately after
meals as required.

These tablets were manufactured by
Messrs Endocrines of 72. Wigmore Street.London.
At my request they most courteously agreed to
inform me of the means by which they prepared
the Adrenal Substance, which is as follows:-

The re-action of the patients to the above prescription was most marked, most dramatically so in one or two cases. The good effect was always obtained within 48 hours, except in the case of the two patients who gave absolutely no re-action at all.

The above prescription appears to have a very rapid action, it produces effects within ten minutes of being taken by the mouth. This is well demonstrated by Cases 3. 4. and 6.

The improvement obtained was always rapid and progressive.

In order to clear up any misunderstanding it may be permitted to side track for a short space.

The use of the term adrenal gland was brought into common use after the discovery of Adrenaline. This change in nomenclature has probably been the factor for a great amount of misconceived ideas with regard to the functions of the Supra renal gland.

Nearly all the text books, both Physiological and pharmacological describe the functions of the supra renal gland as being those of Adrenaline. Text books on Medicine deplore the fact that Adrenaline is of no beneficial effect in Addison's Disease, and that therefore there does not appear to be the same relation between Addison's and Adrenaline, as there is between Myxedema and Thyroid.

In the light of our present knowledge that the Cortex, which does not appear to secrete adrenaline, is essential to life; and that the medulla which does secrete adrenaline is not essential to life, it would be more accurate to state that the functions of the Supra Renal Gland as a whole are still unknown and to describe the functions of Adrenaline under another and separate heading.

The use of the term Supra Renal Gland has therefore been used throughout this paper. It has at least the value of being a correct anatomical description.

This point cannot be stressed too far because from the literature on the supra renal gland there is far too much importance paid to the results as compared with those of the functions of Adrenaline. This occurs in nine clinical papers out of ten; there being in these cases a complete disregard of the cortex.

9 It is for the same reason that the term hypo adrenalism has not been used, and that disfunction of the supra renal gland has been used instead.

In some of the milder cases a complete cure was effected.

In the more severe forms the treatment gives immediate cure but must be continued intermittently to keep the case well. (Case 4). If the condition is still more severe treatment must be carried out continuously; if there is so much as a lapse of

six hours symptoms at once begin to re-appear, but fortunately even in these cases, treatment keeps them in almost perfect health.

Unfortunately there is still another class of case, and these are the two typical cases of Addison's disease which appear in the series. One is dead (Case No.16) but as will be seen from the history she was temporarily very much relieved: the other (Case No.2) takes treatment continuously but although she is very much improved she has remissions of her symptoms.

The subjective effect this treatment has on the patients is most astounding, and the rapidity with which it appears to come on (Cases 1, 2, 4, 6, 9 and 12) is shown very markedly by

It is always the subjective mental symptoms which are relieved first and as a rule the effect is noticed within twenty four hours. The next symptom to improve is the Constipation; this improvement takes place on the average within 72 hours. The hard small dull black scybalous masses to which the patient has been accustomed, even under the influences of purges, are changed into elongated soft dark yellow coloured motions. In nearly all the cases where constipation was present treatment has brought relief. Cases Nos. 2, 3, 4, 6, 11, 16, 17, 24 and 28 had all been habitually constipated for years and had to take daily purgatives, but within 72 hours of the commencement of treatment,

treatment, this was relieved, and has kept relieved without any necessity of taking other purgatives.

The treatment has very definite influence over the pains experienced by Case 2 and 6. In Case 6, the epigastric pain is relieved by a tablet within ten minutes of taking it.

Case 4 has suffered from a very troublesome anuria for years. Since she commenced treatment, this symptom has never re-appeared except once, after treatment had been left off for fourteen days.

This symptom which appears in two or three other cases has always been relieved by treatment.

Treatment had no effect on the pigmentation of Cases 2 and 16.

Sargent's White Adrenal Line was not present in more than 50% of the cases and treatment did not influence it very markedly.

The same can be said about the blood pressure - the findings were far too indefinite to be of any clinical significance, but most cases showed a low reading.

The above prescription as a therapeutic measure is undoubtedly of the greatest value. From a scientific standpoint it lays itself open to several objections.

The first is that the prescription is a "Blunder Bus". The effect which is produced by it might be due to any one of the ingredients contained in it, perhaps the Thyroid might be proclaimed as the only endocrine extract which, when taken by the mouth has any therapeutic effect.

The Prescription was therefore divided up into its component parts. Each part was made into a separate tablet, the exact replica of the parent tablet. This was done in order that there might be no question of psycholological effect on the patients when the tablet was changed.

Tests were now carried out on 2. 4. and 6. as these cases were known to be unable to carry on without the prescription, as symptoms would at once arise if it was withdrawn. The first change which was made was to give each of the three patients tablets containing the Supra Renal Gland. This had undoubtedly an effect. The patients symptoms were all kept in check, but at the end of fourteen days, the patients did not feel so well as they had done on the mixed prescription. There was no appreciable change on the blood pressure or pulse rate or the temperature, Owing to the distance apart of these three patients, it was not practicable to take the Blood Pressure etc oftener than biweekly. The bronzing in Case 2 did not deepen.

The next step was to put them all back on to the old prescription and there was an undoubted improvement. They were allowed to remain like this for one week.

The tablet containing the Thyroid gr 1/12 was next substituted (the patients knew nothing of these interchanges) In all three cases there was a gradual falling off in energy. In case No.6. depression at once re-appeared and at the end of

fourteen days she showed her original picture of neurasthenia. Case No.4. remained fairly well for the fourteen days but had slightly more depression and just towards the end her muscular asthenia and the symptoms of anuria re-appeared.

Case No.2. became so weak that the experiment could only be carried out for six days and the original prescription had to be recommenced at once. In 48 hours she was again in her usual condition of health.

At the end of the fourteen days of Thyroid treatment Case 4 and 6 were given Rx Throid gr 1/12 Supra Renal Gland whole substance gr $\frac{1}{4}$ and both showed a marked improvement, and at the end of three days they had fully recovered from the ill effects produced by taking Thyroid alone. The substitution of the original prescription did not appear to make any difference.

In all these cases the substitution of either the Spermin Extract or the Calcium Glycero-phosphates was followed by a return of the symptoms.

The conclusions arrived at from these experiments are:-

(1). The extract of the Supra Renal gland (whole substance) is by far the most important element in the original prescription.

(2). That although Supra Renal Extract gave good results when used by itself, these results were materially augmented by the addition of Thyroid gr 1/12 (U.S .P.)

(3) That Thyroid gr 1/12 (U.S.P.) did have quite a marked effect in two of the cases, symptoms partially under control but not nearly so well as the Supra renal extract had done.

In case 2 which presents the true Addisonian picture the result of the withdrawal of the Supra Renal gland extract was so disastrous that it was at once recommenced and no further experiments were carried out on this case.

(4) That the Spermin extract has no specific action on the Symptoms of the Symptom Complex.

(5) That Calcium Glycerophosphates has no specific action on this Symptom Complex

The second objection to the original prescription is that we are quite unable to prove that Supra Renal Gland extract is actually present in the prescription as we do not know what the constituents of the extract are and therefore we are unable to test for them chemically. The presence of Thyroid and Adrenaline can be proved, but we must rely on the manufacturer that Supra Renal Gland extract is really present.

An important point in administering glandular extracts is to be certain that they are active, and that the actual principle of the gland had not been destroyed in the process of manufacture.

There is at present no method of standardising the activity of these extracts other than by clinical trial.

If it has been proved that a certain manu-

facturer's preparation is active, it may be assumed that he has a process which does not destroy the activity of the extract. The following case illustrates this point very markedly. It demonstrates how easily one can be deceived with regard to the activity of any gland extract:-

"Mr A. a Station Master has myxoedema; He
"has been in perfect health for the past two years
"whilst taking Thyroid Manufactured by X. For
"some reason Thyroid manufactured by Y was substituted. The same dose being given as before.
"He at once began to develop myxoedematous
"symptoms. The dose of this extract of Y's was
"doubled, trebled, and even quadrupled, but without
"any result being obtained. The patient kept
"steadily getting worse. He was then replaced on
"his original Thyroid manufactured by X in doses
"of gr 5 daily. He became his normal self, within
"three days. This demonstrates that had there
"been any doubt with regard to the diagnosis, and
"had Y'S preparation been tried in the first place
"Thyroid extract would have been condemned for this
"particular case, which would have kept on getting
"worse.

The rapidity of the action of Adreno Spermin Co is in many cases very marked. The following examples bring this out very clearly.

Case No.4. was at the Dairy show in London and about midday she began to feel very tired and

all her old sensations of complete exhaustion were returning; she suddenly remembered she had a 'tablet' in her pocket, took it, and within two minutes she declares her whole sensation of exhaustion had entirely disappeared. She was able to remain for the rest of the day at the Show and returned home in the evening not being unduly tired, and with no sense of exhaustion.

No.6. The pain that this woman suffers in her right hypochondrium is "at once" dispelled by the taking of a tablet ; by "at once" is meant within five minutes , The result is invariably the same.

Her fits of depression are controlled within ten minutes of taking a tablet.

Case No.5. This lady is so uncertain in her sleeping powers that she under no circumstances will attempt to go to bed without her nightly dose of Tablets. These, she says, are always beneficial

Case No.2. Her headaches and attacks of sickness are controlled within ten minutes .It sometimes requires two tablets.

It is typical of nearly all these patients that they at once seem to appreciate the fact that they have forgotten to take their tablets. They all ascribe the sensation which reminds them of their omission as being one of mental exhaustion. It can be safely said of most of these patients, that they are as regular in their taking of the gland as they are

in taking their dinner.

The above observation clearly brings out that the first symptom a patient experiences is one of mental exhaustion, followed quickly by muscular tiredness. There is, with these patients a clear cut distinction between ordinary muscular fatigue and this subjective mental exhaustion.

Professor Stewart makes a scathing comment on the bulk of clinical evidence, which is not deserved. The mere fact that physiologists are unable to reproduce symptoms of the disease should have no weight with clinicians.

It must be admitted at once, that we give the supra renal extract in a purely empirical way.

No objection can be made to this as empirical measures have often won therapeutic success, which had to wait long for scientific explanation, (such as quinine for malaria and mercury for syphitis) and which in some cases have not yet received it (viz Salicylates for rheumatism and colchicum for gout)

The empirical method has always been suspect by the laboratory, but in many instances the laboratory has had reason to be suspicious of the clinicians.

To quote but a few of the examples in which the clinicians have been held up to ridicule by the laboratories, and in which science has long afterwards

proved their experience to have been first rate science:-

(1) Cod Liver Oil was used for many years to the scorn of the experimentalist - until vitamins were discovered and he scoffed no more.

Gull and Ord discovered the functions of the Thyroid at the bed side, when the laboratory made no more helpful suggestion than that it was merely to improve the contour of the neck.

Addison was the first to point out the functions of the Supra Renal Gland, while the role of the pituitary was discovered by the symptoms of acromegaly and Frohlick's syndrome.

It must be remembered that when using the empirical method it is necessary to be particularly critical with regard to the results obtained. Physiologists may have failed in their experiments on Supra Renal Glands in the past because animals may not re-act in the same way to the milder forms of hypo-functions of the Supra Renal Glands. It is proved beyond a shadow of doubt that the gonococcus is the specific organism of Gonorrhoea, yet when it is injected into the Mucous Membrane of the urethra of the monkey, it fails to reproduce any symptoms or signs, but no Bacteriologist attempts to deny the fact that the Gonococcus is not the cause of Gonorrhoea just because they are unable to reproduce the disease experimentally in animals. If the tissues of the monkey fail to re-act to what is known to be a highly virulent infection, how much more likely is it that they will fail to re-act to

mild hypofunction of the Supra Renal Gland.

From an analysis of the symptoms of cases of hypofunction of the Supra Renal Gland, it is found that the earliest symptom is that of mental exhaustion. It would seem to be impossible for experimentalists to measure this symptoms in animals. Thus there is no necessity for physicians to be turned aside from the empirical uses of endocrine extracts, merely because they have not yet been proved experimentally.

There is abundance of clinical evidence that Supra Renal Gland whole gland substance has been very beneficial and this weight of evidence must not be thrown lightly aside. experimental evidence does not prove its worth.

CONCLUSIONS

- (1) That the Asthenic symptom-Complex herein described is a definite Clinical entity.
- (2). That it is definitely related to Addison's Disease and is therefore definitely related to the Supra Renal Gland.
- (3). That this Asthenic symptom Complex can be treated by a Specific Therapy.
- (4). That an extract of Supra Renal Gland whole substance is active by the mouth.
- (5) That the cortex of the Supra Renal Gland is essential to life.
- (6) That the medulla is not essential to life.
- (7) That in view of this fact it is better to revert to the older terminology and to refer to the Gland as the Supra Renal gland.
- (8) That it will be from clinical rather than from experimental knowledge that the functions of the Supra Renal Gland will be more fully discovered.
- (8) That the active principle of any gland extract may be destroyed in the process of manufacture and there is no method of proving that this has happened other than the clinical method.
- (10- Adrenal Sargent's White /Line was not pathognomonic

of the Asthenic Symptoms Complex.

(11) That pathological conditions of the Supra Renal Gland exist in a great number of clinical disease unsuspected, and that sufficient pathological significance is not attributed to the Supra Renal Gland.

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